Allergy Abstracts

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Allergy Abstracts

Announcement

ALLERGY ABSTRACTS has been published since 1936 by members of the Allergy Division of the Jewish Hospital of Brooklyn. The Editorial Board is comprised of former residents of this department who contribute their services.

ALLERGY ABSTRACTS selects and abstracts those articles in the literature which may be of clinical or theoretical interest to workers in the field of allergy. Each abstract represents a summary of the author's findings and views, and its inclusion in ALLERGY ABSTRACTS does not imply approval of its contents by the editor.

—*The Editors.*

Asthma and Hay Fever

Studies in Atmospheric Pollen. II. Diurnal Variation in the Incidence of Grass Pollen. Hyde, H. A., and Williams, D. A.: The New Phytologist **44**: 83, 1945.

A grass pollen survey was conducted at Llandough, near Cardiff, Wales, from June 15 to June 22, 1944. Four sets of slides were exposed. Two were gravity slides in an apparatus somewhat similar to the standard Durham apparatus used in the United States, and two were "impact" slides, attached in a vertical position to a weather vane in such a way as to face into the wind. Two sites were used, one on top of a building, the other near by in the midst of a dense patch of grassy vegetation. Slides were exposed for two-hour periods throughout the day, and observations were made on sunshine, rain, wind direction, and wind velocity. When these data were plotted on a graph, it was found that all four curves moved up and down in unison with no apparent time lag between ground and roof catch. The impact catch was always ten times greater than the gravity catch at the same site. A morning and an afternoon rise were noted at both sites every day. The highest counts occurred following several hours of bright sunshine. On cloudy days, the afternoon counts were relatively low. Variations in the pollen counts were closely related to the times of flowering of the principal grasses in the area, and were more marked on the ground than on the roof site. Low counts during the hours of darkness were correlated with the total cessation of flowering during that period. Thus, there is a diurnal variation in grass pollen counts which can be correlated with the incidence of bright sunshine and with the flowering of the neighboring grasses. The impact catch appeared to be a more sensitive index of grass pollen liberation than the gravity catch. C.

A Daily Census of Alternaria Spores Caught From the Atmosphere at Cardiff in 1942-1943. Hyde, H. A., and Williams, D. A.: Brit. Mycological Soc. **29**: 78, 1946.

A report is presented of studies done at Cardiff, Wales, in 1942 and 1943, on the incidence of alternaria spores as determined by counts made on gravity slides. It was found that alternaria spores form a normal and regular part of the annual spore rain at Cardiff. Although virtually absent during the late

autumn and winter months, they are present in the spring and summer, and in greatest numbers during the months of June through September. The catch during these months totalled 646 spores (89 per cent of the total) in 1942, and 726 (96.5 per cent) in 1943. The period of highest incidence coincided with that of the highest mean temperature. The catch during June, July, and August varied considerably from day to day, probably due to weather changes. There was some correlation between daily catch and maximum temperature. There was no apparent correlation between wind velocity and alternaria catch. Rainfall on certain occasions resulted in a marked, though temporary, diminution in the catch. In order to compare the spore counts at Cardiff with those in the United States, the authors submit the following figures for maximum daily catch and average seasonal total in 1.8 sq. cm., respectively: Greenville, Maine, 25 and 278; McKeever, N. Y., 21 and 350; Yorke, Maine, 16 and 202; Llandough, Wales, 22 and 255. It is believed that the alternaria spores present at Cardiff originate in cereals growing in the vicinity. C.

Cypress Pollinosis in South Africa: A Study of Seasonal Hay Fever and Allergic Conjunctivitis Occurring in the Winter-Spring Period. Ordman, D.: South African M. J. **19**: 142, 1945.

Cypress pollen sensitivity was found to be the specific cause of winter-spring hay fever and allergic conjunctivitis in fourteen cases. The management of these cases is discussed in detail. Desensitization is begun early in April and is continued until the middle of June, when cypress pollination starts. C.

The Effect of Aminophylline on the Prothrombin Time in Man. Breytsbraak, R. W., and Greenspun, F. S.: Am. J. M. Sc. **212**: 476, 1946.

The prothrombin time in a small series of human subjects was found to be unaltered following the administration of large doses of aminophylline orally or intravenously. F.

Penicillin Spray by Bulb Atomizer in Respiratory Infections. Morse, F. W.: J. A. M. A. **132**: 272, 1946.

The simple hand atomizer was found to be an effective instrument for administering penicillin by the spray method. Various types of respiratory infections including pneumonia, bronchitis, sinusitis, laryngitis, and pharyngitis, as well as postoperative atelectasis and middle-ear dsease, were successfully treated by this method. Dosage ranging from 40,000 to 100,000 units given in divided doses every four hours is recommended. F.

Pulmonary Calcifications: Roentgenographic Observations in Relation to Histoplasmin and Tuberculin Reactions. Swerling, H. B., and Palmer, C. E.: Radiology **47**: 59, 1946.

The pulmonary calcifications found in individuals residing in the central-eastern portion of the United States are more often associated with a positive reaction to histoplasmin than to tuberculin. This finding confirms that of Palmer, who conducted an extensive survey among student nurses in eight large cities. It is likely that the histoplasmin reaction is an indication of a previous infection which, contrary to earlier beliefs, is not necessarily serious or fatal. Histoplasmosis in subclinical form is probably widespread. The pulmonary calcifications which it produces closely resemble those of tuberculosis, and necessitate care in making the differential diagnosis. F.

Dermatology

Exfoliative Dermatitis Following Penicillin Therapy. Nolan, D. E., and Pedigo, G. W., Jr.: Ann. Int. Med. **25**: 725, 1946.

Exfoliative dermatitis as a result of penicillin therapy was observed in a Negro man, aged 60 years, who was under treatment for a lung abscess. A course of penicillin was started, following two weeks of sulfadiazine therapy. The patient was receiving 15,000 units of penicillin every three hours. After the fifth dose, generalized itching and urticaria were noted. Within twenty-four hours after cessation of therapy, the lesions disappeared. Fourteen days later, penicillin therapy was resumed, 20,000 units being administered every three hours. After the fourth dose, a diffuse erythema of the skin accompanied by nausea and perspiration occurred. There was no evidence of urticaria. Although penicillin was discontinued, the erythema persisted, and within three days the skin over the involved areas began to exfoliate. This process continued for four weeks. A patch test performed with the penicillin was strongly positive. The saline control was negative. Three weeks later, the patient was tested intracutaneously and by contact with a different brand of penicillin. Negative results were obtained. It was concluded that the exfoliative dermatitis was probably due to some impurity in the original batch of penicillin. This is said to be the first case of exfoliative dermatitis following penicillin therapy reported in the literature. A.

Dermatitis Due to Preparation and Administration of Penicillin Solution. Goodman, H.: Arch. Dermat. and Syph. **54**: 206, 1946.

A 50-year-old physician, who had been administering sodium penicillin for eighteen months, developed vesicular oozing and pruritic eruptions on the fingers which contacted the syringe. When rubber gloves were worn for protection, similar lesions occurred on the wrist where the gloves were grasped for removal. Dermatitis also appeared on the face. Patch tests with sodium penicillin were positive. E. WALZER.

Dermatitis Due to Quinacrine Hydrochloride. Becker, F. T.: Arch. Dermat. & Syph. **54**: 338, 1946.

Vesicular-eczematoid dermatitis, apparently due to sensitivity to quinacrine hydrochloride (Atabrine), was observed in two patients. The initial reaction in each case occurred in the Southwest Pacific following several months of prophylactic atabrine dosage. The eruption was resistant until the drug was discontinued. The rash then gradually disappeared, but in each case malaria ensued. Within forty-eight hours after the institution of therapy with atabrine, all areas of skin previously involved became acutely inflamed. When quinine therapy was substituted for atabrine, the rash improved and gradually disappeared. Since atabrine is a fluorescent dye, it was thought that the drug might have a photosensitizing effect. This could not be demonstrated by exposing the skin to ultraviolet light. J. SHERMAN.

Contact Dermatitis from Penicillin. Friedlander, S., Watrous, R. M., and Feinberg, S.: Arch. Dermat. & Syph. **54**: 517, 1946.

Of five cases of contact dermatitis from penicillin which are reported, four occurred in workers engaged in the manufacture of penicillin, and one in a chemist who was producing the drug by the surface culture method for experimental study. Four of the patients were patch tested. Three showed

reactions to pure crystalline penicillin as well as to intermediary products. The fourth showed negative reactions to crystalline or commercial preparations and positive reactions to the chloroform extract and to mold mycelium. These results indicated that sensitivity was due to substances other than penicillin. None of the four patients showed positive reactions to intradermal tests with mold extracts. E. WALZER.

Neurodermatitic Reaction. Sachs, W., Miller, C. S., and Gray, M. B.: Arch. Dermat. & Syph. **54**: 397, 1946.

"Neurodermatitic reaction" is the term used by the authors to denote the microscopic changes which occur in neurodermatitis. The reaction involves the cutis and epidermis. The latter is acanthotic and regular. The walls of the arterioles and small arteries are thickened, and the vessels of the middle and upper layers of the cutis show focal infiltration composed of small round and wandering cells. The reaction is also characteristic of nummular eczema, exudative lichenoid, and discoid chronic dermatosis. The differential diagnosis of these conditions as well as other similar conditions is discussed. Diagnosis depends upon a careful consideration of the clinical appearance and microscopic findings. J. SHERMAN.

Hypersensitivity to Sunlight and Dysmenorrhea Controlled with Benadryl. Report of a Case. Tyson, W. G.: J. Invest. Dermat. **7**: 209, 1946.

A 32-year-old Negro woman had suffered for five years with chronic urticaria due to hypersensitivity to sunlight. There was severe dysmenorrhea during the menstrual period, at which time the urticaria was intensified. The personal and family history was negative for allergy. Routine skin testing performed by the scratch technique showed only a positive reaction to house dust. All medication previously administered failed to give relief except for the transitory beneficial effect of epinephrine. A daily oral dose of 200 mg. of benadryl controlled the urticaria so that the patient was able to tolerate sunlight. The dysmenorrhea was also alleviated. J. SHERMAN.

A Case of Allergy to Phenylhydrazine. Solomons, B.: Brit. J. Dermat. and Syph. **58**: 236, 1946.

Generalized urticaria following the ingestion of phenylhydrazine was observed in a patient being treated with this drug for polycythemia. The personal and family histories were negative for allergy. A patch test performed with crystalline phenylhydrazine was positive within twenty-four hours. Contact dermatitis from phenylhydrazine has been reported in the literature. The present case is said to be the first recorded instance of urticarial reaction to this drug. A.

Otorhinology and Ophthalmology

Effect of Sulfonamide Drugs on Mucous Membranes. Dickson, J. C.: Arch. Otolaryng. **44**: 474, 1946.

Six new sulfonamide drugs were instilled daily for periods varying from five to fifteen days into the noses of fifteen rabbits. At the end of that time the rabbits were sacrificed, and histologic examinations of the mucous membranes were made. The pH range of the drugs varied from 5.0 to 9.4. None of the drugs (thizodrine, sulfadrine, gluco-fedrin with sulfathiazole, sulfedex, Paredrine sulfathiazole suspension, and sulmefrin) produced any ill effects

on the mucous membranes of any of the rabbits. Since the mucosa of rabbits is similar to that of human beings, it is concluded that these drugs, despite the wide range in pH from 5.0 and 9.4, are not injurious to the epithelium of the nose. C.

Intranasal Medication: An Investigation into the Relative Merits of Certain Methods of Introducing Fluids into the Nose. Cawthorne, T.: Ann. Otol., Rhin. and Laryng. **55**: 519, 1946.

In order to test the relative efficacy of various methods of introducing medication into the nose, both the olfactory and the chemical sense in normal subjects were abolished by the application of cocaine. Four milliliters of 10 per cent cocaine solution were introduced into each nostril of seven subjects by means of drops, spray, sniffing, and in the head-low position. Olfactory tests with nitrobenzol, guaiacol, and xylol were started within two minutes after each test instillation. The chemical sense, i. e., the sensitivity to pungent vapors of that part of the nasal mucous membrane supplied by the Trigeminal nerve, was tested for its reaction to the inhalation of ammonia fumes. It was found that, in the head-low position, olfaction was affected in all instances, being abolished in six cases and diminished in one. With this method the respiratory area was affected in two cases, and sensation was abolished in five cases. It is concluded that, by this technique, a wider area of the nasal mucous membrane could be reached than by drops, spray, or sniffing. C.

Privine Sensitivity: A Report of Eight Cases. Thomas J. W., and Fabiano, U.: South M. J. **39**: 658, 1946.

Eight cases of addiction to the use of Privine hydrochloride as a nasal vasoconstrictor are presented. Clinically, the appearance of the nasal mucous membrane was indistinguishable from that of typical allergic rhinitis. Improvement in each case followed the discontinuance of the drug. Although Privine hydrochloride gave excellent, immediate, local nasal constriction, its use was followed in a few hours by swelling and pronounced nasal obstruction which could be attributed to a secondary vasodilatation involving the deeper venous sinuses rather than the subepithelial vascular bed. This secondary vasodilatation is due either to the presence of an active vasodilator in the drug or to fatigue of the constrictor mechanism. The indiscriminate use of Privine, as well as other nasal vasoconstrictors, is discouraged in both allergic and nonallergic patients. C.

Colloidal Salt Nasal Tamponades: Their Use and Abuse. Wolf, G. D.: J. A. M. A. **130**: 273, 1946.

The use of tamponades saturated with solutions of mild protein silver is of questionable value in the treatment of nasal sinus infections. These solutions stimulate the flow of mucus which may activate harmful bacteria and furthermore possess little antiseptic properties. Other objections to the use of such solutions are the possibilities of inducing Argyria and allergic reactions. Through many years of experience the author has observed that colloidal silver tamponage is of dubious value in purulent sinusitis or in instances of nasal obstruction of a physical nature. Allergic patients are often made worse by its use. There is, however, another type of patient who is frequently benefited by use of these medications. These patients complain of vague headache, nasal stuffiness, and rhinorrhea; are usually somewhat obese, and

often constipated. The appearance of the nasal structures frequently suggests an allergic etiology. Nasal tamponage in these cases is followed by a very profuse mucoid discharge and long-lasting relief after several treatments.
F.

Miscellaneous Allergies

Death Due to Administration of Typhus Vaccine. Rifkin, H.: Ann. Int. Med. **25**: 346, 1946.

Death occurred within twenty-five minutes following the injection of 1 c.c. of typhus vaccine in a white male, aged 24 years. Eight minutes after the administration of the vaccine, the patient complained of severe difficulty in breathing and became extremely cyanotic. Shortly thereafter, he became comatose and pulseless, and expired, despite artificial respiration and the administration of epinephrine. He had never had typhus vaccine previously. There was a past history of nausea, vomiting, and lassitude following the ingestion of either raw or cooked eggs. The odor of eggs caused nausea. An autopsy performed two hours after death showed a severe bilateral and diffuse emphysema, a marked eosinophilia in a thin eosin-staining exudate in the lumina, and eosinophilic infiltration of the walls of the small bronchi and bronchioles. The alveoli were enlarged to four or five times their usual size. The pulmonary pathology was attributed to the tetanic contraction of the bronchial musculature with eventual asphyxia. It is suggested that all patients who are suspected of being egg-sensitive be tested intracutaneously with diluted vaccine before receiving immunizing doses of egg-yolk vaccines.
A.

Pressures Required to Produce Intradermal Wheals in Normal Human Subjects. Moss, W. G., and Pfeiffer, C. C.: Proc. Soc. Exper. Biol. & Med. **63**: 44, 1946.

The pressures required to raise wheals in the skin on the volar surfaces of the forearms were determined in eleven subjects. Wheals were raised with a tuberculin syringe connected through a three-way joint to a glass spoon manometer which had been calibrated against a column of mercury, and to a 27-gauge hypodermic needle introduced into the skin. The pressure in the system was increased rapidly with saline or with histamine solution until a wheal started to form and was held until the wheal reached a diameter of from 5 to 7 mm. Five readings were made each day and averaged. In 160 such determinations, the pressure required to produce wheals varied from 1,000 to 3,200 mm. Hg with a mean pressure of 2,000 mm. Hg. No race or sex factors were found. The average mean deviation of pressure for a given subject in the same day was greater when the bevel of the needle was up than when it was down. More pressure was required to raise the wheals with histamine than with saline solution.
E. WALZER.

Loeffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis): Report of Twenty-six Cases. Wright, D. O., and Gold, E. M.: Arch. Int. Med. **78**: 303, 1946.

Of fifty-two cases of creeping eruption (cutaneous Helminthiasis), twenty-six developed pulmonary lesions of the type found in Loeffler's Syndrome. These patients had the usual paucity of systemic symptoms along with the peripheral eosinophilia observed in Loeffler's Syndrome. In 75.5 per cent of the cases positive skin reactions were obtained with Ascaris and Trichina

antigens. Stool examinations were negative for nematodes and ova. No larvae were found in the sputum. The pulmonary lesions in these cases may have been due to the presence of dead larvae in the lungs, or to the fact that the host was sensitized to exotoxins elaborated by subepidermal larvae. F.

Tuberculin Reactors: An Interpretation and Evaluation of Certain Data. Dash, H. H., Masten, A. R., Taylor, C. F., and Levin, O. S.: Am. Rev. Tuberc. **54**: 159, 1946.

The various tuberculin skin testing techniques should not be evaluated solely on their ability to produce a maximal number of positive reactions. Many "nonspecific reactions" may be provoked with the use of 0.005 mg. of PPD, since a number of persons showing positive reactions to this dose manifest no evidence of tuberculous disease. For tuberculosis survey work, therefore, the two-dose Mantoux technique has no practical advantage over the use of either an intermediate PPD dose of 0.0001 mg. or the transcutaneous techniques. Old tuberculin may give nonspecific reactions due to the presence of extraneous material mixed with the tuberculin. It is suggested that "nonspecific" reactions to PPD may be based on a person's contact with acid-fast organisms other than the tubercle bacillus. There is no tuberculin testing technique which will give 100 per cent screening of persons with tuberculous disease. It is not known why some tuberculous individuals fail to show a cutaneous reaction to tuberculin. E. KAILIN.

Systemic Reactions to the Intravenous Administration of Congo Red. Selikoff, I. J., and Bernstein, I. J.: Quart. Bull. Sea View Hosp. **8**: 131, 1946.

During the course of 100 consecutive congo red absorption tests, severe systemic reactions occurred in six patients following the intravenous administration of small doses of the dye. Two deaths occurred. These reactions may be related to the hemostatic properties attributed to congo red. Since each of the patients had had previous injections of congo red without untoward symptoms, the reactions might have been in the nature of an anaphylactic response to the readministration of the dye. Although congo red, an azo dye, is not a protein, it may act as a sensitizing agent by coupling with the patient's own serum to form an azoprotein. The danger of intravenous injection of congo red, particularly in the arteriosclerotic age group and in those who have previously had the dye, is stressed. No case of reaction to the first administration was observed. C.

Periarteritis Nodosa Complicating Scarlet Fever. Peale, A. R., Gildersleeve, N., and Lucchesi, P. F.: Am. J. Dis. Child. **72**: 310, 1946.

Periarteritis nodosa developed after the third week of scarlet fever in an 11-year-old boy with a history of food allergy. The patient died of an intracerebral hemorrhage and renal failure. At autopsy the vascular lesions were widely distributed throughout the organs of the body. There was no gross evidence of nodulation, although numerous petechial and macular hemmorhages were seen. This case report is presented as additional support to the assumption that periarteritis nodosa may be an allergic manifestation of varied causation. C.

Tuberculin Allergy in Patients Critically Ill with Tuberculosis. Woodruff, C. E. Am. Rev. Tuberc. **53**: 583, 1946.

Cutaneous tuberculin tests with graded strengths of Old Tuberculin were done on 54 adult persons on their admission to a tuberculosis sanatorium. The

tests were repeated at weekly intervals when these patients became critically ill. It was found that the patients who maintained their skin sensitivity to 1:1,000 or higher dilutions of the tuberculin died either from hemorrhage or silico-tuberculosis, whereas those who exhibited a decline in their reactivity died of widely disseminated tuberculosis. Usually several months were necessary for the titer to fall from the 1:10,000 level generally found on admission to the 1:1,000 level, but from this point on the decline was rapid and complete loss of responsiveness often occurred within three weeks. The rapid decline in skin reactivity to tuberculin was usually observed only a few weeks before death. Of 33 patients who had a skin titer of less than 1:1,000 terminally, none died of hemorrhage. E. KAILIN.

Henoch-Schonlein Purpura and Acute Nephritis Due to Food Allergy. Brown, A. Glasgow M. J. **27:** 84, 1946.

A case of acute hematuria and Henoch-Schonlein purpura in a boy, aged 9 years, was traced to specific sensitivity to tomato. Positive skin tests to tomato were obtained, and the elimination of tomato from the diet prevented the recurrence of attacks. However, red blood cells and casts were still present in the urine three months after the last attack. C.

Treatment of Migraine by Intravenous Histamine. Thomas, W. A., and Butler, S. Am. J. of Med. **1:** 39, 1946.

A series of carefully selected cases of severe migraine was treated by the slow intravenous administration of 1 mg. of histamine base in 500 c.c. of physiologic saline. The treatments were given on six successive days and over a period of three to eight hours or more. Blood pressure readings were taken at frequent intervals, and the rate of flow of the medication was adjusted according to any pressure or symptomatic changes. Of 104 cases comprising this series, 42 had complete and permanent relief, 16 had complete relief for a temporary period, 34 had partial relief, and 12 failed to experience any relief. Patients with hypertension, gastric ulcer, cardiac, renal, mental, or central nervous system diseases are unsuitable for this type of treatment. F.

Necrotizing Arterial Lesions Resembling Those of Periarteritis Nodosa and Focal Visceral Necrosis Following Administration of Sulfathiazole. Report of a Case. Lichtenstein, L., and Fox, L. J.: Am. J. Path. **22:** 665, 1946.

During the open reduction of a dislocated shoulder in a 61-year-old Negro woman, 5 Gm. of sulfathiazole was dusted into the wound. Nine days later, the patient experienced a chill, her temperature rose to 103° F., and a vesicular eruption appeared. Although there was no evidence of wound infection or of septicemia, the patient received 31.5 Gm. of sulfathiazole over a six-day period, after which penicillin was substituted. The patient expired three weeks after the operation, with manifestations of uremia, associated with liver damage and hyperbilirubinemia. At autopsy, four types of lesions were found: focal necrosis of the liver, lung, myocardium, spleen, gall bladder, and pancreas; necrotizing arterial lesions similar to periarteritis nodosa in the kidneys, liver, spleen, gall bladder, adrenals, uterus, and Fallopian tubes; parenchymal degeneration of the liver and kidneys; and acute fibrinous pleuritis with bilateral patchy bronchopneumonia. Some eosinophiles were found in the arterial and focal necrotic lesions. It was concluded that the

initial sensitization was induced by the introduction of sulfonamide into the clean wound. No other fatality following this route of hypersensitization is said to have been reported. E. WALZER.

A Case of Serum Sickness Treated with Procaine Intravenously. Applebaum, E., Abraham, A., and Sinton, W.: J. A. M. A. **131**: 1274, 1946.

A 16-year-old boy complaining of inability to open his mouth was suspected of having tetanus. Further investigation revealed that the patient was suffering from serum sickness following the use of tetanus antitoxin. Temperomandibular arthralgia accounted for the trismus. Intravenous treatment with 1 Gm. of procaine in 500 c.c. of isotonic sale solution, given over a period of two hours, gave excellent results.

Anaphylaxis

The Antigenicity of Alkali-Treated Bovine Serum Protein. Kazal, L. A., DeFalco, R. J., and Arnow, L. E.: J. Immunol. **54**: 245, 1946.

Bovine serum was exposed at room temperature to 1N sodium hydroxide for varying periods of time up to twenty-four hours. The alkali-treated proteins were recovered from the digests by iso-electric precipitation. After treatment up to two hours, the proteins reacted weakly with the antiserum for untreated bovine serum. The proteins subjected to alkaline treatment for four hours or longer failed to react with the same antiserum. The antigens obtained with treatment up to eight hours stimulated the production of antibodies, whereas the protein treated for longer periods of time lacked antigenicity as shown by precipitin tests, anaphylactic studies, and complement fixation determinations. Alkaline digestion beyond twelve hours deprived the antigen of its haptenic properties. With the loss of antigenicity, toxicity appeared. Guinea pigs succumbed to the intravenous injection of relatively small amounts of bovine serum treated with alkali from twelve to twenty-four hours, while injections of large quantities of two-to-eight-hour-treated material failed to produce similar effects. J. SHERMAN.

Antihistamine and Autianaphylactic Effect of Hetramine. A New Synthetic Pyrimidine Compound. Feinstone, W. H., Williams, R. D., and Rubin, B.: Proc. Soc. Exper. Biol. & Med. **63**: 158, 1946.

The toxicity as well as the antihistaminic and antianaphylactic properties of Hetramine N, N-dimethyl-N′ benzyl-N′ (a-pyrimidyl) ethylene-diamine were studied in laboratory animals. The acute toxicity in LD_{50} was between 62.5 and 75 mg/kg of mouse weight when Hetramine was administered subcutaneously and between 300 to 500 mg/kg when administered orally. Administration of 50 mg/kg orally or 20 mg/kg subcutaneously did not affect the hemoglobin or growth of young rats. As little as $\frac{1}{16}$ of 1 γ per c.c. of Hetramine counteracted the muscular contractions of guinea pig ileum produced by 1 γ of histamine per c.c. in the Dale bath. The pretreatment of guinea pigs with 4.0 to 6.0 mg/kg Hetramine intraperitoneally or with 10 times that dose orally thirty minutes before the intracardiac administration of 0.85 mg/kg of histamine insured the survival of the animals. Similarly, the mortality of guinea pigs could be significantly reduced when from 0.3 mg/kg to 2.5 mg/kg of Hetramine was administered intraperitoneally before the animals were exposed to the vapor of 5 c.c. of a 0.125 per cent solution of histamine. In anaphylactic experiments, it was found that 6 mg/kg of

Hetramine intraperitoneally was needed to protect seven of eight guinea pigs sensitized with horse serum, against an intracardiac shocking dose of the antigen. E. WALZER.

Influence of the Liver in Anaphylactic Shock: An experimental Study. Grana, A.: Ann. Allergy **4**: 261, 1946.

The usual fall in blood pressure and other signs of anaphylactic shock are not observed when the liver is excluded from the circulation of sensitized dogs. When sensitized livers are transplanted into normal dogs and these animals are injected with the antigen, anaphylactic shock occurs and there is a loss of blood coagulability. During anaphylactic shock, liver histamine is decreased in proportion to the severity of the reaction, and blood histamine rises. Nevertheless, when isolated sensitized livers are perfused with the antigen, no increase in the histamine content of the perfusion fluid has been noted. The foregoing phenomena may be duplicated by the intravenous injection of hydatid fluid or ascaris extract into normal dogs and by the perfusion of normal isolated livers with these substances.

Blood to which antigen has been added is not coagulable when it is perfused through a sensitized liver. When anaphylactic shock is produced in liverless dogs, there is no increase in the blood heparin. Protamine, which combines with heparin in vitro neutralizes the anticoagulant in anaphylaxis. Hence, the liver is the most important organ in the production of anaphylaxis in the dog and in shock produced by certain parasitic extracts. This organ, in vivo, is largely responsible for the fall in blood pressure and the liberation of heparin and histamine which occur in these reactions. E. WALZER.

Antihistaminic Substances in Histamine Poisoning and Anaphylaxis of Mice. Mayer, R. L., and Brousseau, D.: Proc. Soc. Exper. Biol. & Med. **63**: 187, 1946.

Mice are very resistant to histamine poisoning. They tolerate 1,000 times as much as guinea pigs. Whereas 0.6 to 0.8 mg/kg injected intravenously killed guinea pigs instantly, 375 mg/kg was lethal for only 43 per cent of mice. When 25 mg/kg of Pyribenzamine or Benadryl was combined with 375 mg/kg histamine, the mixture was fatal to 100 per cent of the mice. Although the mortality of horse-serum-sensitive mice to specific tests was 89 per cent, this figure was reduced to 65 per cent when 10 to 50 mg/kg of pyribenzamine was injected just prior to the administration after twice the shocking dose of antigen. Some of the mice which had received 50 mg/kg of pyribenzamine undoubtedly died from the toxic effects of the drug, since the LD_{50} for mice is 75 mg/kg of body weight. Hence, although antihistaminic substances act as synergists in histamine poisoning of mice, they have some protective power in anaphylaxis in this animal. It is suggested that, in the mouse, histamine affects organ systems other than those in histamine-sensitive animals, and in these points of attack, the antihistaminic substances are unable to compete with histamine. The protection afforded by pyribenzamine against anaphylaxis is probably due to pharmocologic properties other than its antihistaminic power. E. WALZER.

Myotropic Spasmolytic, Histaminolytic, and Atropine-Like Actions of Some Derivatives of Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl). Winder, C. V., Kaiser, M. E., Anderson, M. M., and Glasseo, E. M.: J. Pharmacol. & Exper. Therap. **87**: 121, 1946.

Several new salts of the basic "benadryl" radical were found to have actions similar to the hydrochloride in counteracting histamine shock in

guinea pigs and inhibiting intestinal strip contractions induced in vivo by barium chloride, acetylcholine and histamine. Quarternary ammonium derivatives of the base appeared to exert greater inhibition of acetylcholine-induced contractions than benadryl, while retaining their property of histamine antagonism. The relationship of molecular structure of the compound to the inhibition of muscle contractions induced by various excitants is discussed.

E. KAILIN.

Miscellaneous

Clinical observations on the Use of Benadryl: Its Effect On Histamine-Induced Gastric Acidity in Man. McElin, T. W., and Horton, B. T.: Gastroenterology **7**: 100, 1946.

Gastric analyses were performed on eight subjects with multiple sclerosis who were receiving histamine subcutaneously and intravenously. Benadryl was administered intravenously, orally, or intramuscularly. An attempt was made to evaluate its effect on gastric acidity. The results obtained were difficult to analyze since they were not entirely consistent. There was suggestive evidence, however, that the curve of gastric acidity was altered by benadryl. In order to demonstrate this, it was necessary to reduce the stimulating dose of histamine to a low order and to administer benadryl parenterally. In one instance, benadryl seemed to produce a rise in gastric acidity. The effect of benadryl on normal gastric acidity was not investigated. A.

Benadryl Fails to Protect Against Histamine-Provoked Ulcer. Friesen, S. R., Baronofsky, I. D., and Wagensteen, O. H.: Proc. Soc. Exper. Biol. & Med. **63**: 23, 1946.

The effect of benadryl on the gastric secretory response to histamine and its protective effect on histamine-provoked ulcers were investigated in dogs. Benadryl failed to affect the gastric secretory response to histamine in forty experiments. Neither the volume nor the acidity of the secretion was decreased when benadryl was administered before histamine was given. On the contrary, there was some evidence that benadryl enhanced the histamine response. When benadryl in beeswax was administered daily, simultaneously with histamine in beeswax, to seven dogs, all developed gastric and/or duodenal ulceration. In two control animals receiving only benadryl in beeswax, one showed early gastric erosions and the other showed no pathology. Animals treated with both drugs became more debilitated than those receiving histamine alone. The failure of benadryl to produce a consistent decrease in gastric secretion indicates that it is not a specific antagonist to histamine, but that it counteracts some of the effects of histamine by virtue of its own pharmacologic action. A.

A Case of Agranulocytosis Occurring During the Course of Penicillin Therapy. Spain, D. M., and Clark, T. B.: Ann. Int. Med. **25**: 732, 1946.

Prior to a cecostomy, penicillin therapy was instituted on a white male, aged 54 years. After the operation on the following day, a generalized erythematous macular rash was noted. This was attributed to penicillin sensitivity. On the third day postoperatively, the temperature rose sharply and a white blood count of 2,800 with 15 per cent polymorphonuclear leucocytes was found. The following day the count dropped to 100 cells with no polys. Penicillin was discontinued, a transfusion was given, and sulfadiazine therapy was instituted. About sixteen hours after the penicillin had been dis-

continued, the white cell count rose to 6,000 with a normal percentage of polymorphonuclear leucocytes. A few days later, when the patient died, the white count had risen to 10,700. In addition to penicillin, several other drugs had been given; namely, morphine, scopolamine, vitamins K and C, demerol, and phenobarbital. It was not considered likely that the other medications had any causal relationship to the onset of the agranulocytosis, since the same medications were continued during the agranulocytosis and were also given afterwards without any effect on the white blood count. Furthermore, the rise in the white count after cessation of penicillin therapy appeared to be significant. A.

The Partition of Potassium Between the Isolated Lung of the Dog and Its Perfusate with Particular Reference to the Action of Adrenaline. Hebb, C., and Nimmo-Smith, R. H. J. Physiol. **105**: 1, 1946.

Freshly isolated, blood-perfused, ventilated dog lungs were studied to determine the exchange of potassium between the lung tissue and the circulating blood under various conditions. The opposite lung of the same animal served as a control. Lung tissue was found to lose potassium to the plasma after ten minutes of ischemia. Inflation of the lungs with air under positive pressure also produced an elevation in the plasma potassium level, and this effect was immediate and reversible. Epinephrine (10 to 50 micrograms) caused the exchange of potassium from the lung parenchyma to the plasma. Increasing the pulmonary arterial tension did not affect the potassium values. The type of response of bronchial smooth muscle to epinephrine varied with the plasma level of potassium. The broncho-constrictive effect of epinephrine on the isolated lung preparation after a two-hour stabilization period occurred when the plasma potassium level was low and the lung tissue concentration of this ion was high. When the plasma potassium level was increased by inflation, ischemia, a previous epinephrine injection, or by phosgene poisoning, epinephrine caused broncho-dilatation. It is not known whether the plasma potassium changes are directly instrumental in affecting the response to epinephrine or whether a more fundamental tissue response is responsible. E. KAILIN.

The Release of Antibody by Sensitized Antigens. Jenkins, C. E.: Brit. J. Exper. Path. **27**: 111, 1946.

Union between B. typhosis and its antibody at low temperatures is rapid. The rate of union varies with different organisms, and the amount of antibody taken up by the antigen varies inversely with the temperature. At 56° C., antibody is released from an antigen-antibody complex. An optium method of preparing a concentrated solution of released antibody is described. Released antibody is distinguished from normal antiserum by the fact that it is not filterable through fine grain porcelain and is not dializable. After treatment with ethyl alcohol, a suspension of antigen was mixed with its homologous antiserum and was found to absorb antibodies. The washed suspension agglutinated normal homologous serum. Upon heating at 56° C., the alcoholized antigen suspension was found to release part of the absorbed antibody. Evidence is presented which suggests that the released antibody is a globulin. J. SHERMAN.

Allergy Abstracts

Asthma and Hay Fever

Principles and Practice of Aerosol Therapy of the Lungs and Bronchi. Abramson, H. A.: Ann. Allergy **4**: 440, 1946.

An aerosol is a relatively stable suspension of solid or liquid particles in any gas. Two factors determine the therapeutic efficacy of an aerosol, the size distribution of the particles and the stability of the mist. The size of the aerosol particles determines the extent to which they will be taken up by the respiratory tract. Particles of 3 micra and larger are completely taken up, whereas particles of 1 micron and larger are taken up by the lung to the extent of 97 per cent. As particle sizes become smaller, more are recovered on expiration. The Vaponephrin and DeVilbiss nebulizers with suitable appliances are recommended for therapy since the mass of their particles are 0.5 micron or greater in radii. "Droplets of solution which do not contain materials to lower the vapor pressure diminish rapidly in size after leaving the nebulizer, and absorption is variable because of the unpredictable particle size distribution of smaller particles." The addition of glycerol to most solutions stabilizes the particle size distribution. When strong solutions of penicillin are nebulized, the penicillin itself tends to stabilize the particle size distribution. The value of the rebreathing apparatus in aerosols is questioned.

Epinephrine, penicillin, streptomycin, sulfonamide, and hydrogen peroxide aerosols are discussed, and a brief review of the literature is presented. Penicillin aerosol was administered to a limited number of patients with chronic suppurative lung disease for two to four days. This was followed by hydrogen peroxide aerosol as such, or in the form of urea peroxide aerosol containing 10 per cent glycerol for two days. The results indicate that this combined form of therapy may be an important aid in treating such cases. The presence of catalase in the sputum of one of these patients led to a search for a suitable anticatalase, to be added to the peroxide to retard the effect of the enzyme. It is suggested that hydrogen peroxide aerosols will probably be of value in reducing secondary infection in advanced tuberculosis and as a prophylactic in the prevention of secondary infection in early tuberculosis. E. WALZER.

Loeffler's Syndrome: Report of a Case With Pathologic Examination of the Lungs. Baggenstoss, A. H., Bayley, E. C., and Lindberg, D. O. N.: Proc. Staff. Meet., Mayo Clinic **21**: 457, 1946.

A case report is presented of a 59-year-old woman with asthma of seven years' duration. Abnormal and atypical roentgenographic markings were observed in the lungs. On autopsy the histologic findings consisted of large numbers of eosinophilic leucocytes in the pneumonic exudate, advanced organization of the exudate with fibrosis and giant cells, the presence of peculiar granulomatous lesions, and the occurrence of necrotizing arteritis and phlebitis. These findings suggest that there is an underlying allergic basis in Loeffler's syndrome. C.

Botanical Survey of Southern California. Small, W. S., and Small, G. M.: Ann. Allergy **4**: 352, 1946.

The results of a botanical survey of California lying south of latitude 35 is presented. Among the allergenic plants, the weeds most commonly encountered were: *Artemisia californica* (Coast Sagebrush), *Artemisia vulgaris hetero-*

phylla (California Mugwort), *Artemisia tridentata* (Mountain Sagebrush), *Ambrosia psilostachya* (Western Ragweed), *Atriplex lentiformis* (Lenscale), and *Salsola kali* (Russian Thistle). The common allergenic grasses included: *Cynodon dactylon* (Bermuda Grass), *Distichlis spicata* (Salt Grass), *Sorghum halepensis* (Johnson's Grass), *Poa annua* (Annual Blue Grass). The allergenic trees most commonly observed were: *Quercus agrifolia* (Coast Live Oak), *Quercus chrysolepis* (Canyon Oak), *Quercus dumosa* (Scrub Oak), *Platanus racemosa* (Sycamore), *Juglans californica* (Southern California Black Walnut), *Juglans negra* (Black Walnut), *Juglans regia* (English Walnut), *Olea Europaea* (Olive), and *Populus fremontii* (Cottonwood). Although southern California has a wide variety of potential excitants of hay fever, pollen counts in urban areas are relatively low. E. WALZER.

Insulin Shock Treatment of Bronchial Asthma. Godlowski, Z.: Brit. M. J. **4453**: 717, 1946.

Eleven cases of bronchial asthma, eight "allergic" and three "nonallergic," were subjected to insulin shock therapy. Seven of the eight allergic individuals experienced complete disappearance of symptoms for periods as long as two and one-half years without relapse. The remaining cases had transitory relief for five months after which time symptoms recurred. The three "nonallergic" cases failed to respond to the treatment, except that during the shock itself they all were relieved of dyspnea for a few hours. During shock a marked increase in blood pressure was noted. This form of treatment is therefore contraindicated in hypertensive patients. Patients with impaired carbohydrate tolerance should not be subjected to insulin therapy.

The explanation for the improvement obtained is that the procedure artificially stimulates the adrenal glands causing a hyperproduction and increased dissipation of epinephrine. It is difficult to explain the long lasting effect of this form of therapy. However, the results of animal experimentation indicate that the adrenals are markedly hypertrophied by such shock and that the medulla of the gland works in an emergency manner to liberate adrenalin only when stimulated either by nervous impulses or toxic agents such as insulin. F.

Treatment of Bronchial Asthma With Small Doses of Copper. Klaarenbeek, F. W.: Nederl. tijdschr. v. geneesk. **90**: 730, 1946.

Favorable results were obtained in seven young adults suffering from bronchial asthma by the injection of a copper preparation. The recommended dosage at weekly intervals was 10 mg. for the first dose, 25 mg. for the second dose, and 50 mg. thereafter. When the maximum beneficial effect had been obtained, the intervals were increased to two and four weeks. C.

Bronchial Asthma in the Young Male Adult: A Study of Fifty Patients Returned From the Tropics for Bronchial Asthma, as Compared to Fifty Asthmatics Stationed in the United States. Rosen, F. L.: Ann. Allergy **4**: 391, 1946.

Of fifty soldiers who had spent an average of six months in the Southwest Pacific and were evacuated to the United States for asthma, 40 per cent had their initial attacks overseas. Of a similar group of fifty asthmatic soldiers who had never left the United States, only 14 per cent had the onset of their disease after induction. Of the tropical group, 32 per cent had blood eosinophilia, whereas 42 per cent of the United States group showed similar findings.

About 83 per cent of both groups showed negative roentgenograms of the chest. Intracutaneous skin testing revealed more reactions to timothy in the tropical group, than in the United States group. On the other hand, the latter group had more positive reactions to ragweed, feathers, and foods than the former. The positive reactors to molds were few, but equal in the two groups. No comparison was made of past personal or family history of allergy. E. WALZER.

Dermatology

Reactions to Penicillin. Vogel, H. R.: Arch. Dermat. & Syph. **54**: 713, 1946.

Two severe reactions following the administration of penicillin are described. The first patient was being treated for a recalcitrant pustulosquamous dermatitis of the palms and soles. He was given 25,000 units of penicillin every three hours. After the sixth dose, he complained of itching of the face and hands. After the eighth dose, erythema of the face and neck developed followed by vesicles on the face and arms. After the ninth dose, penicillin therapy was discontinued. Exfoliation of all the involved areas occurred three days later. The second patient had a pustular follicular eruption of the neck of three months' duration. He had received two previous courses of penicillin parenterally without improvement. He was therefore given a cream containing 100,000 units of penicillin in 60 Gm. of cetyl alcohol base. Within twenty-four hours, he developed mild itching of the extremities and urticaria. The ointment was continued for another twenty-four hours. At this time the patient became semicomatose. He showed marked edema of the entire face and giant wheals covered the entire body. Râles were heard at both bases and the pulse rate rose to 150. The patient gradually recovered within forty-eight hours. Intracutaneous tests with penicillin were negative. The author warns against the indiscriminate use of the drug. A.

The Treatment of Penicillin Urticaria With Nicotinic Acid. Service, W. C.: Ann. Allergy **4**: 397, 1946.

Among forty-one cases with allergic reactions to penicillin, urticaria was the most prominent symptom encountered in thirty-seven. Contact dermatitis occurred in three cases and eczematoid dermatitis in one. The urticaria was associated with angioneurotic edema of the face in twelve cases, with angioneurotic edema of the genitalia in two and with signs and symptoms of serum sickness in three. Temporary relief, in some instances, was obtained by the use of epinephrine, ephedrine, calcium gluconate, vitamin K, morphine, or benadryl. In thirty-seven patients complete relief of all symptoms followed within twenty-four hours after the intravenous injection of 35 mg. of nicotinic acid dissolved in 10 c.c. of distilled water. Four patients required a second injection. E. WALZER.

Immunological Studies on Patients Developing Urticaria Associated With Penicillin Therapy. Callaway, J. L., and Barefoot, S. W.: J. Invest. Dermat. **7**: 285, 1946.

Urticaria associated with the administration of penicillin therapy may occur at any time in the course of therapy or after its termination. Complete immunologic studies were made on five patients who developed urticaria as a result of penicillin therapy. Intracutaneous tests which were performed with a normal saline solution containing 20,000 units of sodium penicillin per ml. within twenty-four hours after the urticaria had subsided were all negative at thirty minutes, twenty-four hours, and forty-eight hours. Passive transfer

studies performed with the sera of these patients also yielded negative results. Sites previously sensitized with these sera could not be activated by the injection of penicillin in distant areas of the body. Reversed passive transfer studies were negative. Precipitin tests performed with the sera of four of the subjects yielded positive ring tests with the penicillin solutions. Similar precipitates were obtained with the sera of normal controls. In two instances, the penicillin employed in these studies was from the identical lot which had caused the patient's clinical reaction. In all cases, the urticaria was successfully controlled with benadryl. A.

Recurrent Vesicular Eruption of the Hands Due to Food Allergy. Flood, J. M., and Perry, D. J.: J. Invest. Dermat. **7**: 309, 1946.

Thirty cases of recurrent vesicular dermatitis of the hands are attributed to food allergy. Three cases are presented in detail. The offending foods were detected by administering a purgative, starving the patient for one day, and then adding one new food each day to the diet. Prompt improvement occurred in all cases on elimination of the offenders and definite exacerbation of the skin lesions occurred within several hours after its ingestion. Fish, wheat, milk, tomato, pork, lamb, pineapple, eggs, chocolate, and chicken were found to be frequent offenders. Not all cases were caused by food allergy, some being attributed to contact allergens, fungi, and psychosomatic factors.

J. SHERMAN.

The Treatment of Dermatoses With Benadryl (Beta Dimethylaminoethyl Benzhydryl Ether Hydrochloride). An Analysis of Its Effects Upon 170 Patients With Various Dermatoses. Goldberg, L. C.: J. Invest. Dermat. **7**: 301, 1946.

The effect of benadryl on various dermatoses associated with pruritus was studied. Acute and chronic urticaria, dermographism, and angioneurotic edema responded well. Atopic dermatitis improved subjectively but not objectively. In herpes zoster, the pruritus disappeared and the pain diminished. Dermatitis medicamentosa was definitely improved. The pruritus disappeared and the offending drug could be better tolerated. The results in dermatitis venenata were not consistent. The only case of dermatitis herpetiformis which was studied responded well. Varying degrees of success were obtained in controlling the pruritus associated with a variety of skin conditions, such as seborrheic dermatitis, pityriasis rosea, anal and scrotal pruritus, dermatophytosis with "id" reactions, insect bites, miliaria, exfoliative dermatitis, and postscabetic pruritus. The effect of benadryl was transitory and symptoms recurred after the drug was discontinued. Side reactions occurred, the most common one being drowsiness. J. SHERMAN.

"Fixed" Eruption of the Mucous Membrane and the Skin Caused by Sulfadiazine. Cole, L. M.: Arch. Dermat. & Syph. **54**: 675, 1946.

Fixed eruptions of both the skin and mucous membranes were observed following the administration of sulfadiazine. All three patients were American soldiers who gave histories of having had similar lesions following the administration of sulfadiazine on previous occasions. Each of the three individuals showed denuded inflamed areas on the buccal membranes and bullous or vesicular lesions on the shaft of the penis. After the lesions had healed, acute exacerbations were induced in each case by the ingestion of sulfadiazine. Patch tests performed with sulfadiazine powder were negative. A.

Use of "Benadryl" for Penicillin Urticaria. Wilcox, R. R.: Brit. M. J. **4480**: 732, 1946.

Five cases of urticaria caused by penicillin and one by luminal were treated with benadryl. Satisfactory results were obtained in all but one penicillin case. The total dosage given each case ranged from 150 to 450 milligrams. The patient who was unsuccessfully treated received an additional injection of ten minims of adrenalin and suffered a severe reaction consisting of pallor, rapid thready pulse, collapse, pyrexia, and leucocytosis. F.

Atopic Dermatitis of the Hands Due to Food Allergy. Rowe, A. H.: Arch. of Dermat. & Syph. **54**: 683, 1946.

Of 182 patients with "Eczematoid" dermatitis of the hands the primary etiologic factor in 80 was food allergy. The ratio of females to males was more than four to one. The average age for both sexes was in the twenties. The dorsum of the hands and sides of the fingers were the most frequently involved areas, and the average duration of the lesions was seven years. Most of the rashes were perennial in nature. Manifestations of food allergy were associated with the dermatitis in 38 per cent of the cases, and a positive family history of allergy occurred in 35 per cent. The most common offenders among the foods were eggs and fruit. Positive reactions to scratch tests with foods were obtained in less than 10 per cent of the cases. The diagnosis of food allergy was usually made with elimination diets. Pollen allergy was a secondary factor in 24 per cent of cases. Excellent results were obtained in 46 cases and good results in 34 by local therapy and the elimination of offending foods. Irritation of the skin of the hands by household duties or by other occupations and avocations helps "to activate a potential sensitization to food in the skin." E. WALZER.

Clinical Uses of 2-3 Dimercaptopropanol (Bal): Skin Sensitization to Bal. Sulzberger, M. B., Baer, R., and Kanof, A.: J. Clin. Investigation **25**: 488, 1946.

It was found that 2-3 dimercaptopropanol (British Anti-Lewisite) possesses the ability to sensitize both intact and injured human skin. The BAL produced neither the classic eczematous contact type nor the classic urticarial type of skin sensitivity, but rather an erythema with edema and papules which were largely, but not entirely, confined to the area of exposure. Subjects previously exposed to Lewisite were more prone to develop sensitivity to BAL than were unexposed persons. Patch tests on sensitized individuals suggested that there was an antigenic cross-relationship between BAL and at least two other chemically related compounds. Sensitivity to BAL as demonstrated by patch tests was also produced after repeated intramuscular injections, but no flare-up of previously sensitized sites could be elicited by a single large intramuscular dose. F.

Erythema Multiforme with Special Emphasis on Postvaccinal Erythema. Schwartz, M. H., and Brainerd, H. D.: J. Pediat. **29**: 513, 1946.

The allergic nature of erythema multiforme is suggested by the fact that three of six cases observed by the writers had a personal history of allergy. Three of the cases followed smallpox vaccination and were believed to be the result of an antigen-antibody reaction. In another case with a rheumatic disease background, erythema multiforme was thought to be due to streptococcal sensitivity. A fifth case followed the administration of horse

serum and was an accompaniment of serum sickness. Four of the six patients had mucous membrane lesions in the mouth and to a lesser degree in the conjunctivae. The buccal lesions consisted of a grayish membrane which wiped off easily and left a bleeding surface. The authors consider these mucous membrane lesions pathognomonic of erythema multiforme. F.

Contact Dermatitis. An Analysis of All Cases Proved in a Single Year. Howell, J. B.: Arch. Dermat. & Syph. **53**: 265, 1946.

In a twelve month period, the author was able to prove the cause of contact dermatitis in 250 cases. Topical medicaments were found to be the most frequent single cause of contact dermatitis. Sulfonamides and mercurials were the most potent sensitizers. The topical application of a drug for some trivial eruption often resulted in a contact dermatitis which was commonly mistaken for an infection such as cellulitis. Contact testing with sulfonamides is discouraged because of the danger of aggravating existing eruptions. The oral administration of a small dose of sulfonamide is recommended as a test. Many cases of occupational dermatitis were observed. Among farmers, ranchers, and oil field workers a high incidence of hypersensitiveness to weeds and plants was encountered. When avoidance of contact was impossible, the offending plant oils were administered orally with excellent results. Among the unusual cases was a housewife who developed dermatitis whenever she used knife handles made of Cocobolo wood. Another patient was sensitive to honey which he contacted in his occupation. A barber developed contact dermatitis from bay rum. A dental assistant handling artificial dentures developed a dermatitis from carbon tetrachloride. Another dental assistant with eczema of both hands proved to be sensitive to ethylene glycol. Many other case histories are included. A.

Mango Dermatitis and Its Relationship to Poison Ivy Hypersensitivity. Kiel, H., Wasserman, D., and Dawson, C. R. Ann. Allergy **4**: 268, 1946.

A case of contact dermatitis due to Mango fruit is presented. This eruption develops about the lips and chin following ingestion of the fruit and on the fingers, dorsum of the hands, and forearms in those who pick the fruit. Patch test studies with various parts of the fruit show that the excitant is in the stem sap which often contaminates the external surface of the peel. The pulp and juice are innocuous. A relationship exists between Mango and poison ivy dermatitis. These plants are members of the same family. A previous history of poison ivy dermatitis is frequently found among those contracting Mango dermatitis. Persons sensitive to poison ivy are apt to become sensitized to Mango fruit on adequate exposure. Persons sensitive to poison ivy should avoid contact wth the Mango fruit either as pickers, handlers, or consumers. J. SHERMAN.

Plant Dermatitis in the Bahamas. Jackson, W. P. U. Brit. Med. J. **1**: 298, 1946.

The author calls attention to the presence of the shrub Metopium toxicoferum, "poison wood" or "poison bark," in the Bahama Islands and southern Florida. The plant contains a toxin at least as powerful as that of Rhus toxicodendron, and produces severe clinical symptoms when it comes in contact with the skin. The widely distributed skin lesions are believed to be manifestations of a general allergic cutaneous reaction resulting from systemic dissemination rather than from spread by contact. F.

Otorhinology and Ophthalmology

Contact Testing of the Buccal Mucous Membrane With Special Reference to Penicillin. Goldman, L., and Farrington, J.: Ann. Allergy **4**: 457, 1946.

Two cases of penicillin stomatitis are reported. One followed topical application to an ulcerative gingivitis. In the other the stomatitis was associated with a severe exfoliative dermatitis which resulted from parenteral administration of the drug. Four patients with facial dermatitis due to penicillin who showed positive cutaneous patch tests also gave positive buccal mucosa contact tests. Two other patients with dermatitis following parenteral administration of penicillin showed positive intracutaneous and buccal mucosa contact tests. Normal controls were negative. Despite the frequent use of penicillin by oral administration, by topical application in the mouth, or by aerosolization, stomatitis from its use is uncommon. J. SHERMAN.

The Nature of the Action of Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl): Effects Upon the Human Eye. Harris, R., McGavack, T. H., and Elias, H.: J. Lab. & Clin. Med. **31**: 1148, 1946.

The pupillary size remained unchanged in twenty subjects who received benadryl orally in doses of 150 to 400 mg. daily. Sixty subjects were given topical applications of 0.5 per cent aqueous solution of benadryl in one eye. In forty-eight, the pupillary size increased, becoming maximal in one hour and decreasing in two hours. In four patients dilatation persisted for more than twenty-four hours. The untreated eye was not affected. Visual acuity decreased in twelve subjects, and remained unchanged in forty-eight. Accommodation of the treated eye was diminished in forty-three of the sixty patients, the opposite eye remaining unaffected. Benadryl dropped into the eye one hour after homatropine had been instilled caused a slight additional dilatation in thirteen of fifteen patients. Benadryl also increased the dilatation caused by epinephrine. Pupillary constriction induced by physostigmine was partially counteracted by benadryl in ten of fifteen patients. Benadryl has an atropine-like effect (vagal paralyzant) when topically applied to the eye. K.

Report of a Death From Pontocaine Hydrochloride. Ahroon, W. A.: Laryngoscope **56**: 320, 1946.

Death ensued in a 27-year-old white woman following a second local application of 2 per cent pontocaine prior to bronchoscopy. The first application had been made ten days previously. Pontocaine has fifteen times the anesthetic power of cocaine, but is two and one-half times as toxic in the same concentration. In the case under discussion it is believed the patient developed a sensitivity following the first application of the drug. There is no known test which will reveal such a sensitivity. Reactions occur more often in allergic persons than in normals. C.

Vascular Basis of Allergy of the Eye and Its Adnexa. Duggan, W. F.: Arch. Ophth. **36**: 551, 1946.

A comprehensive and critical review of the literature covering allergic manifestations in the eye is presented. Allergy of the eye is considered as a problem in vascular physiology, since, with the exception of the muscles of the iris and the ciliary body, most of the smooth muscle in the eye is found in the walls of the arteries and arterioles. Allergic reactions of the ocular tissues are regarded as manifestations of localized vascular dysfunction which causes

areas of localized tissue anoxia. Vasodilator therapy, which relieves tissue anoxia is therefore recommended in the treatment of allergic lesions of the eye. C.

Miscellaneous Allergies

Allergic Sensitization to Penicillin: Experimental Results. Chu, W. C., and Cutting, W. C.: Proc. Soc. Exper. Biol. & Med. **63**: 347, 1946.

Normal guinea pigs and rabbits were tested intracutaneously with crystalline penicillin G for pre-existing sensitivity. Of eleven guinea pigs, two developed small wheals which lasted twenty-four hours. One rabbit in a group of twelve showed a similar reaction. Forty animals were divided into several groups and crystalline penicillin was introduced by various routes. It was not possible to produce generalized sensitization in guinea pigs with penicillin.

Local skin sensitization of the Arthus type was investigated in rabbits. The animals received repeated intracutaneous or subcutaneous injections of pure crystalline penicillin G or commercial calcium penicillin. Arthus-like reactions of varying degrees of severity were readily produced. The size of the reaction appeared to depend upon the size of the dose rather than upon the route of administration.

An Arthus-like reaction was observed in a male physician, aged 40 years, who had injected himself subcutaneously with 300,000 units of commercial penicillin in oil and beeswax on two occasions. Subsequently he had taken twenty-five doses of commercial penicillin intramuscularly. Following the twentieth dose, urticaria and red swellings appeared at the sites where the penicillin in oil had been previously injected. The lesions were orange-blue in color, painful, and looked as though they would become necrotic. The reactions subsided when the intramuscular injections were discontinued. It is suggested that penicillin may act as a haptene in combination with body proteins and produce sensitization. Commercial penicillin does not appear to be a more potent sensitizer than pure crystalline penicillin. The skin is apparently the most important shock organ in penicillin sensitivity. A.

Clinical Aspects of Polyarteritis Nodosa. Miller, H. G., and Daley, R.: Quart. J. Med. **15**: 255, 1946.

A comprehensive review of the literature on polyarteritis (periarteritis) nodosa is presented. The etiology, pathology, and clinical manifestations are discussed and nine case histories are presented. The condition is essentially a destructive inflammatory, necrotizing panarteritis involving the small elastic arteries with a tendency to healing by scarring, and to occasional aneurysm formation. The symptoms are protean, depending upon the location of the pathologic involvement, and no single clinical finding is invariably present. Males are more often affected than females in the ratio of three to one. It may occur at any age, but is most common in the third decade. Six to twelve months is the average length of illness, and recovery may occur with little or no residual disability. Almost any organ may be involved, but the kidneys are most commonly affected. The symptoms and signs most frequently encountered are fever, tachycardia, polymorphonuclear leucocytosis, elevated sedimentation rate, anemia, albumin and blood in the urine, hypertension, edema, abdominal pain, and painful neuritis. Blood eosinophilia occurs in less than 20 per cent of cases. Although the diagnosis is usually made post mortem, it is recently being made ante mortem. Experimental evidence has been presented, indicating that the condition represents a hypersensitive reaction. There is suggestive clinical and pathologic evidence that such poorly understood condi-

tions as Loffler's syndrome, Libman-Sacks disease, and lupus erythematosus represent localized forms of acute arteritis, analogous in nature and etiology to periarteritis nodosa. J. SHERMAN.

Treatment of Migraine by Intravenous Histamine. Thomas, W., and Butler, S.: Am. J. Med. **1**: 39, 1946.

Satisfactory results have been obtained in 104 cases of migraine treated with intravenous histamine. All cases in which the diagnosis was doubtful were rejected. One milligram of histamine base in 500 c.c. of saline was given slowly by intravenous drip on six successive days. This procedure is potentially dangerous. It may increase gastric acidity or cause collapse from a fall in blood pressure. It is therefore suggested that it be employed only in severe cases. The treatment is contraindicated in patients with peptic ulcer, hypertensive, cardiac, or renal disease. It is believed that patients with migraine have a lowered tolerance for histamine, and that treatment raises the tolerance. The intravenous drip method appears to be more effective in producing this result than repeated injections. J. SHERMAN.

The Quantitative Lepromin Test in Leprosy. Salazar Mallen, M., and Rosas Prieto, L.: Ann. Allergy **4**: 379, 1946.

Groups of 34 lepromatous lepers, 21 tuberculoid lepers, and 46 nonlepers were tested intracutaneously with 0.1 c.c. of Mitsuda's antigen in concentrations ranging from 1 to 100 per cent. The skin responses were read at the end of one, two, seven, fourteen, and twenty-one days. It was found that those responses showing the most intense reactions at forty-eight hours were most likely to develop necrosis at the end of two or three weeks. The tuberculoid group responded most intensely within two days, and showed a high percentage of necrosis at the end of three weeks. The response of the lepromatous lepers was the least severe, and that of nonlepers was intermediate. Considering the forty-eight-hour response of nonlepers as normergic, the tuberculoid group was found to be hyperergic, and the lepromatous group anergic. It is suggested that having adopted these criteria for the Mitsuda reaction, it is possible to consider it "within the group of tuberculin (infectious) type of allergy." E. WALZER.

Severe Allergic Reactions to Penicillin. Mendell, T. H., and Prose, P. H.: Am. J. M. Sc. **212**: 541, 1946.

Of 5,000 patients treated with penicillin, only six (0.12 per cent) developed reactions sufficiently severe to warrant discontinuance of the drug. Four of the six cases had immediate reactions, two had reactions of the delayed type resembling serum sickness. All cases made an uneventful recovery. Intracutaneous tests gave positive reactions of the immediate type in two of the cases, and patch tests were positive in the three cases in which they were tried. Conjunctival, passive transfer and precipitin tests were negative in all cases studied. Intracutaneous and conjunctival tests with commercial penicillin were made on 200 healthy patients in an attempt to detect those individuals who might react unfavorably to the drug. Fifty per cent of these subjects had received penicillin prior to the experiment. Following the testing each patient was given 50,000 units of penicillin parenterally. None of the subjects who gave positive reactions in the preliminary tests developed evidence of penicillin sensitivity following the parenteral dose. Patch tests appeared to be of greater prognostic significance than intracutaneous tests, but the time element involved makes this procedure impractical. F.

Passive Transfer of Local Allergic Hypersensitiveness to Tuberculin. Corper, H. J., and Stoner, R. E.: Am. Rev. Tuberc. **54**: 305, 1946.

Intracutaneous tests were made on normal guinea pigs and on tuberculo- (tuberculin) allergic hypersensitive guinea pigs with mixtures of blood from normal or tuberculo-allergic guinea pigs with or without tuberculin. The reactions observed were no different from those produced by blood or tuberculin alone in the same animals. There was no evidence that tuberculin mixed with blood from tuberculo-allergic guinea pigs produces a substance toxic to normal guinea pigs, or sufficiently affects the normal tuberculin reaction in tuberculo-allergic guinea pigs to be of value in determining the existence of a tuberculo-hypersensitive condition by means of the blood. K.

Death Following Exposure to DDT. Hill, W. R., and Damiani, C. R.: New England J. Med. **235**: 897, 1946.

A 47-year-old white man had been exposed, while at work, to a spray containing a 6 per cent solution of DDT in kerosene. He had inhaled the fumes and his perspiring skin had contacted the solution. The following day he developed an extensive pruritic eruption on the trunk and extremities accompanied by dyspnea and an unproductive cough. During the next five weeks the cough and dyspnea became progressively worse, and frequent injections of adrenalin were required for relief. At the time of hospitalization, there was a generalized eruption consisting of numerous discrete reddish-purple maculopapules with excoriated surfaces. Hemorrhagic lesions were noted in some areas of the skin. The thorax was emphysematous and coarse râles and ronchi were heard in the chest. The anterior cervical and inguinal lymph nodes were palpable. The white blood count was 43,000 with 20 per cent eosinophiles. A presumptive diagnosis of periarteritis nodosa was made. Specimens removed from cutaneous lesions on the arm and leg were reported as periarteritis nodosa. The patient's condition became progressively worse, and he expired twenty-five days after admission. At autopsy numerous petechiae were found in the bowel and kidneys. Several infarcts were also present in the kidneys. The lungs and other organs showed numerous pathologic changes, but the exact cause of death could not be determined. It is suggested that DDT may act as a sensitizing agent and may cause dermatitis and asthma. It should be included among the drugs capable of producing periarteritis nodosa. A.

A Study of the Incidence of Allergy in Children With Rheumatic Fever. Rittwagen, M., Romano, F. J., and Suigals, M. P.: Arch. Pediat. **63**: 639, 1946.

The incidence of allergy among one hundred children suffering from rheumatic fever was compared with that among one hundred nonrheumatic children. Complete personal and family histories were taken as to the presence of hay fever, asthma, food sensitivity, and vasomotor rhinitis. Thirty-three per cent of the rheumatics had a personal history, and 31 per cent a positive family history of allergy. Only 8 per cent of the controls had positive personal histories, and 10 per cent had positive family histories. Twenty-one per cent of the rheumatics had hay fever, 12 per cent food allergy, 10 per cent vasomotor rhinitis, and 5 per cent bronchial asthma. It was concluded that the incidence of allergy was three times greater among rheumatic children than among nonrheumatic controls. A.

Pulmonary Filariasis. Rifkin, H., and Eberhard, T. P.: Ann. Int. Med. **25**: 324, 1946.

A case of a South Pacific Island native whose clinical history, roentgenologic and laboratory findings suggested a diagnosis of pulmonary filariasis is presented. Numerous microfilariae characteristic of Wuchereria Bancrofti and many eosinophiles were found in the sputum and peripheral blood. A skin test with Dirofilaria Immitis antigen gave a positive reaction in a titer of 1:8,000 and 1:16,000. Filarial lymphangitis is considered to be allergic in nature. When there are sufficient amounts of protein liberated from the desintegration of dying or dead worms, the typical inflammatory manifestations of filariasis result. C.

Comparative Value of Tuberculin Tests. Deane, E. H. W.: Lancet. **1**: 162, 1946.

Forty (80 per cent) of fifty known Mantoux positive children tested with fresh Vollmer tuberculin patch tests showed positive reactions. Only eight (16 per cent) of these children tested with patch tests, eleven months old, showed positive reactions. Forty Mantoux positives were patch tested with a tuberculin jelly; only thirty-five (87.5 per cent) showed positive reactions. Rubbing the skin lightly with a very fine sandpaper prior to the application of the jelly produced a positive reaction in all forty children. The author considers both the Vollmer patch test and the patch test with tuberculin jelly unreliable. H.

Pulmonary Calcifications: Roentgenographic Observations in Relation to Histoplasmin and Tuberculin Reactions. Swerling, H. B., and Palmer, C. E.: Radiology **47**: 59, 1946.

The pulmonary calcifications found in individuals residing in the central-eastern portion of the United States are more often associated with a positive reaction to histoplasmin than to tuberculin. This finding confirms that of Palmer, who conducted an extensive survey among student nurses in eight large cities. It is likely that the histoplasmin reaction is an indication of a previous infection which, contrary to earlier beliefs, is not necessarily serious or fatal. Histoplasmosis in subclinical form is probably widespread. The pulmonary calcifications which it produces closely resemble those of tuberculosis and necessitate care in making the differential diagnosis. F.

Allergy and Allergic Disease. Capuani, Minerva Medica, Turin, p. 829, 1945.

A new method of testing for specific sensitivity is presented. Sensitivity is "transferred" passively from humans to guinea pigs by the injection of 10 milliliters of the allergic patient's serum into the peritoneum of a guinea pig. Twenty-four hours later intestinal strips of the "sensitized" guinea pig are suspended in a Dale bath and tested first with a 1:5,000,000 solution of histamine. If the strip contracts it is washed, the Dale bath is renewed, and testing with allergens is performed as follows: Varying dilutions of an allergenic extract are added to the bath. If no response results, other extracts are similarly tested until a positive contraction is obtained. The same section of intestinal strip may be used for further tests after washing and renewing the bath. The above method may be simplified by "sensitizing" the intestine alone. This is done by bathing the intestinal strip for thirty minutes in the patient's serum. C.

Anaphylaxis

Histamine and Anaphylactic Shock in the Mouse. Perry, S. M., and Darsie, M. L., Jr.: Proc. Soc. Exper. Biol. & Med. **63**: 453, 1946.

Anaphylactic shock was regularly induced in white mice sensitized with intraperitoneal injections of egg white. Shock symptoms consisted of sluggishness, unsteady gait, dyspnea, cyanosis, paralysis of extremities, loss of sphincter

control, convulsions, and death. Of fifty-three mice sensitized to egg white, forty-nine showed some anaphylactic reactions, and, of these, fourteen died in shock. Attempts to produce histamine shock in mice were unsuccessful. Thirty-five mice, injected intravenously with toxic doses of histamine diphosphate, showed no evidence of histamine shock. A series of twenty-five mice, sensitized to egg white, were divided in two groups. The first was injected intravenously with egg white, followed within five minutes by histamine. The second was injected with histamine, followed within five minutes by egg white. The results in both groups were similar to those obtained when the antigen alone was used as the shocking agent. It was apparent that the susceptibility of mice to anaphylactic shock and their resistance to histamine shock could not be explained on the basis of an antihistamine substance in mouse serum. Guinea pigs injected intravenously with histamine incubated with normal mouse serum showed the same degree of histamine shock as those injected with histamine alone. Mouse serum, therefore, did not detoxify histamine for guinea pigs. Guinea pig serum mixed with histamine failed to produce shock when injected into mice. Guinea pig serum, therefore, did not make histamine toxic for mice. The authors concluded from these studies that histamine does not play a role in anaphylactic shock in the house. A.

Intradermal Spread of Vital Dye in Anaphylaxis and Bacterial Allergy. Birkhaug, K., and Böe, J.: J. Immunol. **54**: 107, 1946.

During the first few hours after the introduction of Pontamine Sky Blue into the skin of normal guinea pigs, the spread of the dye is sharply delineated. Later on, the borderline is determined with difficulty. Groups of guinea pigs were sensitized with multiple intracutaneous injections of tubercle bacilli (B.C.G.) or staphylococcic vaccine or by the intravenous administration of horse serum. At various intervals, the sensitized animals were tested intracutaneously with small quantities of Pontamine Sky Blue (Vital dye) mixed with tuberculin, staphylococcic vaccine, or horse serum. The anaphylactic guinea pigs continued to receive intravenous injections of horse serum in order to correlate the development of anaphylactic sensitization and the diffusion of vital dye in the skin. It was found that the bacterial sensitized animals exhibited a marked inhibition of the spread of dye before the sensitization reached its height. The anaphylactic animals likewise exhibited the same restricting influence on the spread of dye before anaphylaxis could be demonstrated by the usual methods. Specific desensitization eleminated the capacity to restrict the spread of dye. Hence "Bacterial allergy and serum anaphylaxis induce a similar change in the organism which restricts the spread of vital dye in the skin." E. WALZER.

Studies of the Acetylcholinergic Action of Antigens and the Acetylcholine Character of Anaphylactic Shock. Nicolau, C. T., and Cristesco, N.: Bull. de L'Acad. de Med. de Roumanie **4**: 10, 1945.

In man, the intravenous administration of horse serum, antigonococcic vaccine, or acetylcholine resulted, within thirty minutes in a leukopenia with an increase in the number of eosinophiles and monocytes. The intravenous administration of 3 c.c. of a 1:100,000 solution of histamine resulted in a leukocytosis without eosinophilia or monocytosis. These findings are presented as further evidence of the acetylcholine-like action of antigens and of the acetylcholine nature of anaphylactic shock. C.

Allergy Abstracts

Asthma and Hay Fever

The Action of Histamine on the Respiratory Tract in Normal and Asthmatic Subjects. Curry, J. J.: J. Clin. Investigation **25**: 785, 1946.

Histamine, administered intravenously and intramuscularly to patients with varying degrees of chronic bronchitis, emphysema, and asthma, caused definite bronchoconstriction as evidenced by diminution in the vital capacity in eight of nine cases. The degree of bronchoconstriction was closely correlated with the dose of histamine administered, but results varied with the patient and with the severity of the asthma. During any single period of observation, the same degree of bronchoconstriction could be produced by identical amounts of histamine introduced by either the intravenous or intramuscular routes. Bronchoconstriction was more severe and more rapid in onset after intravenous than after intramuscular injection. The height of the reaction occurred thirty seconds after intravenous injection and two to three minutes after intramuscular injection. Histamine given sublingually or by nebulization resulted in definite but less pronounced bronchoconstriction. Similar studies were conducted on a control group of ten normal individuals and on a group of ten patients having histories of severe allergic tendencies, including asthma. No significant reductions in the vital capacity were noted in the controls after the intramuscular or intravenous administration of histamine. F.

The Effect of Antihistamine Substances and Other Drugs on Histamine Bronchoconstriction in Asthmatic Subjects. Curry, J. J.: J. Clin. Investigation **25**: 792, 1946.

Bronchoconstriction, as evidenced by decrease in vital capacity, can be produced by the parenteral administration of histamine in certain asthmatic patients. The effect of the antihistaminics, benadryl and pyribenzamine, upon this bronchoconstrictive activity of histamine was studied. Benadryl administered intravenously in doses of ten and thirty milligrams afforded excellent protection against bronchoconstriction. Pyribenzamine administered orally in fifty milligram doses conferred an irregular protection which was slow in onset. The two preparations were not compared on the basis of similar routes of administration. Atropine gave fair protection while aminophyllin, ephedrine, and epinephrine afforded excellent protection against histamine bronchoconstriction. F.

Pyribenzamine in Hay Fever and Other Allergic Disorders. Friedlaender, A. S., and Friedlaender, S.: J. Lab. and Clin. Med. **31**: 1350, 1946.

Side-effects consisting usually of drowsiness, nausea, and vertigo occurred in 27 per cent of two hundred allergic patients given 50 to 100 mg. doses of pyribenzamine four times daily (or 25 to 50 mg. per dose for children). One patient developed urticaria which was definitely attributable to pyribenzamine; three complained of increased nasal stuffiness; and one experienced asthma. Hay fever patients who had had little or no specific desensitization were given pyribenzamine. Of twenty-eight cases of grass pollinosis, nineteen were symptomatically improved. Of seventy ragweed sufferers, twenty-six were benefited when the pollen count was high, twenty were improved on low

pollen days only, and twenty-four were not helped. The greatest proportion of patients aided was in the subgroup classified as having minimal symptoms. Only two of thirty nonseasonal asthmatics obtained symptomatic relief with pyribenzamine, although the concomitant allergic rhinitis was improved in a number of instances. Of one hundred and eight cases of allergic rhinitis, sixty-nine were benefited. Various types of pruritus were relieved, but four cases of vernal conjunctivitis and two cases of allergic headache were not affected by pyribenzamine. E. KAILIN.

Unusual Side-Effect From Benadryl. Weil, H. R.: J. A. M. A. **133**: 393, 1947.

A 3½-year-old boy was given two 50 mg. doses of benadryl for relief of hay fever symptoms. Six hours later, a third dose, consisting of 100 mg. of the drug, was administered. Twenty minutes later, the child was found siting up in bed, singing, and laughing. There were muscular twitchings of the face and involuntary spastic movements of the extremities. Urinary incontinence soon followed. Within a few minutes, the child became irrational. The speech became slurred; exaggerated patellar and triceps reflexes were noted. After administration of a sedative, the child slept fitfully for some hours. Examination of the patient the next day showed him to be normal and with no memory of the events of the preceding night. Since this episode, the child has tolerated benadryl without apparent side-effects. F.

Danger With Benadryl of Self Medication and Large Dosage. Borman, M. C.: J. A. M. A. **133**: 394, 1947.

Two 50 mg. capsules of benadryl per day were prescribed for the treatment of hay fever and asthma in an 18-year-old female. Excellent relief was obtained the first day, and the patient was encouraged to increase the dose herself. During the following three days, forty capsules (2,000 mg.) of benadryl were ingested. The patient became drowsy and irrational. Her temperature, pulse, respiratory rate, and blood pressure remained normal. Treatment consisted of forcing fluids, especially strong coffee. Recovery was complete in forty-eight hours. The patient's judgment may have been affected by the first two capsules of benadryl, thus accounting for the unusual number of capsules subsequently taken. F.

Dermatology

Reactions to Penicillin. Procaine Hydrochloride Intravenously in the Treatment of Reactions Similar to Serum Sickness. Dressler, S., and Dwork, R. E.: J. A. M. A. **133**: 849, 1947.

A 42-year-old woman who had been receiving penicillin and sulfathiazole developed a serum sickness type of reaction. Benadryl controlled the itching and to some extent the skin rash, but failed to relieve the arthraglia and muscle pain which were part of the reaction. The intravenous administration of 1 Gm. of procaine hydrochloride in 500 c.c. of isotonic salt solution immediately relieved the arthraglia and caused the rash to disappear. Within twenty-four hours, the patient was free of all symptoms. Penicillin was thought to be the cause of the reaction, although a patch test with the drug was negative. F.

Rhus Dermatitis. As a Public Health and Health Education Problem. Turner, C. F.: Am. J. Public Health **37**: 7, 1947.

Estimates based upon United States Public Health Service figures indicate that the incidence of Rhus poisoning is 2.5 cases per 1,000 population or 350,000

cases per year throughout the United States. The incidence of the dermatitis runs much higher among the youth in localities where the plant is profusely distributed. Poison ivy, oak, and sumac are actually all of a single genus (rhus or toxicodendron) and perhaps one species. The plants are pleomorphic and take on different forms in different localities. Studies have shown that urushiol, the active agent in the plant, is a nonvolatile oily resin which can only be carried on particulate matter, such as soot, and by insects, animals and inanimate objects. The idea that some persons have a natural immunity to the plant poisoning is incorrect. Such cases are actually instances of allergy and desensitization due to maintained or repeated exposures. Preventive procedures and oral and intramuscular desensitization have been proved to be of little value in the condition. The use of the chemicals 2,4-D or ammonium sulfamate offer the greatest hope for controlling Rhus dermatitis. These herbicides have been effectively employed by several large communities. Cooperation between Health departments and government and community agencies in educating the public in the use of the weed killers can prevent a quarter of a million cases of ivy poisoning a year. F.

Otorhinology and Ophthalmology

Radiation Therapy for the Removal of Adenoid Tissue. Proctor, D. F.: Arch. Otolaryng. **45**: 40, 1947.

Surgical adenoidectomy is very often unsatisfactory because it is almost impossible to eradicate all the nasopharyngeal lymphoid tissue. Furthermore, the mucous membrane which grows in over the denuded nasopharynx contains lymphoid tissue as an integral part of its stroma. Under the stimulus of infection or of allergy, the minutest nodules of lymphoid tissue are capable of growing rapidly to large size and re-exciting bronchial asthma on an infectious basis. The author reports on 400 patients who received, in addition to other indicated nose and throat treatment, a total of 1,110 radon treatments of the nasopharynx for eradication of lymphoid tissue. There was a follow-up period of thirteen months. Good results were obtained in the treatment of deafness due to chronic interference with the function of the Eustachian tubes. Patients suffering from recurrent infections of the upper respiratory tract and recurrent and acute infections of the ear were also benefited. Of nineteen patients with bronchial asthma, nine ceased to have attacks and five others were markedly improved. The technique of the radium treatment is described in detail. C.

Clinical Signs of Diagnostic Importance in Conjunctivitis. Thygeson, P.: J. A. M. A. **133**: 437, 1947.

Although bacteriologic and pathologic examinations are of prime importance in determining the etiology of conjunctivitis, these methods are frequently unavailable to the practitioner. In such an event, careful clinical examination alone can be relied upon for differentiating many of the major types of conjunctivitis. Preauricular adenopathy and many types of blepharal, conjunctival, limbal, and corneal changes are of diagnostic importance. Follicles involving chiefly the upper limbal region are pathognomonic of active trachoma. When these follicles absorb, they leave cicatrices which appear as clear areas on the serrated limbal margins and are known as Herbert's pits. In vernal catarrh the temporal and nasal areas of the limbus are predominately involved but occasionally the entire limbus is ringed with papillary excrescences. This characteristic type of hypertrophy is pathognomonic of the limbal variety of vernal catarrh except that in mild cases it may resemble the

hypertrophy occurring in phlyctenular conjunctivitis or in episcleritis. Chalky concretions known as Tranta's spots which occur in the limbal hypertrophy may also be considered diagnostic of vernal catarrh. The palpebral variety of vernal catarrh is characterized by the presence of pavement blocklike papillas in the upper tarsal conjunctiva in contradistinction to the microscopic type of papillary hypertrophy which has a velvety appearance and is commonly observed in many other types of conjunctivitis. F.

Chronic Nasal Obstruction. Its Causes and Treatment. Thacker, E. A.: J. A. M. A. **131**: 1039, 1946.

Intensive allergic studies were made on one hundred and six sensitive individuals whose chief complaint was chronic nasal obstruction. Sensitivity to inhalants and ingestants was about equally divided, with 50 per cent of the patients showing sensitivity to both groups. Associated allergic disturbances such as gastrointestinal upsets, asthma, and headache were frequently noted. Seventy per cent of the patients had nasal smears showing more than 15 per cent eosinophiles. There was no correlation between the number of eosinophiles in the blood and in the nasal smear. Only 3 per cent of the series gave negative skin reactions but the allergic etiology was confirmed by symptomatology, history, and elimination diets. Pale, boggy turbinates may be diagnostic of an allergic etiology and polyps are a frequent finding. Sinal changes are more common in the long-standing cases of nasal allergy and the degree of sinal involvement appears to parallel the length of time the allergy has existed. Haziness of all the paranasal sinuses is positive proof of an existing allergy; in infectious cases, only one sinus or a unilateral group shows cloudiness. Hypertrophy of the tonsils and adenoids is common in allergic children and control of the allergy must be accomplished before surgery is undertaken. Proper treatment of nasal allergy should include nasal sprays, aminophyllin, nadin, and benadryl orally, plus elimination of offending allergens, specific desensitization and conservative nasal surgery when indicated. If these measures fail, nonspecific desensitization with histamine or histamine azoprotein and/or the instillation of a sclerosing agent into the turbinates may be necessary. F.

Miscellaneous Allergies

Some Aspects of Histamine Metabolism. Rose, B.: Camsi J. October 11, 1946.

Histamine is derived from the amino acid histidin by decarboxylation of the latter and is widely distributed in the blood and tissues. It is a powerful vasodilator, increases capillary permeability, stimulates contraction of smooth muscle and is a powerful stimulant of gastric secretion. It is apparently excreted by the kidney and inactivated in the kidney, lung, and liver by an enzyme histaminase. Both the adrenal medulla and cortex are involved in the regulating mechanism of histamine metabolism. Histamine is released from tissue cells by such stimuli as toxins, venoms, acute burns, as well as in anaphylaxis in animals and in allergic conditions in the human. That anaphylaxis is the counterpart of allergy in man has been evidenced by: (1) the demonstration of an antibody antigen reaction; (2) the demonstration of a release of histamine by cells; (3) the use of antihistamine compounds. The following antihistamine substances and their clinical application are discussed in detail: (a) biologicals, e.g., adrenalin, histamine, amines, and amino acids; (b) synthetics, e.g., atropine, aminophylline, ephedrine, histamine azoprotein, thymoxyethyldiethylamine, antergan, benadryl, pyribenzamine, anthallan, and neoantergan. The injection of increasing doses of histamine diminishes the

sensitivity of the body to this substance, either by desensitization of the tissues, by hyperactivity of the adrenal cortex, or by increasing histamine destruction by histaminase. Evidence would indicate that antigen antibody reactions produce tissue lesions which result in the liberation of histamine. The mechanism, however, remains obscure. It is likely that allergic symptoms result from the liberation of histamine and not from the presence of antigen. C.

The Migrainous Personality and Constitution. The Essential Features of the Disease: A Study of 500 Cases. Alvarez, W. C.: Am. J. M. Sc. **213**: 1, 1947.

Based on his observations of 500 cases of migraine in a thirty-five year period, the author has come to the conclusion that this condition is a specific brain disease dependent upon an inherent predisposition which is likely to remain with the patient throughout life. Correction of physical defects elsewhere in the body has little effect on the condition. The severity of the attacks depends upon the patient's psychic make-up and the strain under which he lives. The typically migrainous person is of a peculiar physical, mental, and spiritual make-up. An overwhelming number are women who tend to be somewhat short in stature, with a trim, well-proportioned body, and better than average looks. The eyes are bright and expressive. The face is intelligent and the responses and movements are quick. In patients not currently suffering with headaches but complaining of abdominal distress, vomiting, or dizzy spells, a diagnosis of migraine equivalent can be made in the presence of the usual migrainous temperament, the typical family history, and the history of cyclic vomiting in childhood. These patients are usually hypersensitive to light, sound, and smell. They tend to worry, to tire easily, and to sleep poorly; they are perfectionists, who are easily upset. Many of these patients have periods of mild depression and detachment from the world and are hazy in their thinking. Many of them have marital difficulties. The disease varies in intensity and is influenced by such factors as allergy, hypertension, dysmenorrhea, psychopathy, or constitutional inadequacy. Psychotherapy, rest, reassurance, elimination of tensions and worry are the most effective therapeutic measures. F.

Extreme Insulin Resistance: A Case Study. McGavack, T. H., Klotz, S. D., Vogel, M., and Hart, J. F.: J. Clin. Endocrinol. **6**: 747, 1946.

A 65-year-old, mildly diabetic white male with cirrhosis of the liver and a chronic fibrotic pancreatitis experienced three episodes of insulin resistance within a seven-year period. The last episode was complicated by a retention cyst of the pancreas. During periods of resistance, the administration of insulin was followed by severe local reactions and generalized urticaria. Reagins for insulin were demonstrated by the passive transfer technique during the last episode. The reagin titer was greater during periods when the diabetes was not under control. The presence of an "insulin neutralizing substance" could not be demonstrated by tests in mice. The hepato-pancreatic pathology is regarded as an additional factor in producing and maintaining the insulin resistant state. E. WALZER.

Insulin Inhibition by Serum of Insulin Resistant Patient. Felder, F.: J. Clin. Endocrinol. **6**: 339, 1946.

Insulin resistance was observed in a 79-year-old, mildly diabetic female following the amputation of a gangrenous foot. The resistance persisted and the patient eventually developed gangrene in the stump and a suppurating

decubitus ulcer. An average of 400 to 500 units of insulin per day was required to control the diabetes. No evidence of allergic reaction was noted following the administrations of large doses of insulin. Studies made on blood obtained immediately after death failed to reveal the presence of precipitins or reagins. Insulin antagonism in the serum was successfully demonstrated in mouse experiments. Serum obtained from the patient, during a period when insulin had been withheld for twenty-four hours, protected nine out of ten mice against insulin convulsions, whereas, serum withdrawn during the time when insulin had been administered freely protected only seven out of fourteen mice. Insulin resistance may be overcome by administering sufficient quantities of the hormone. E. WALZER.

Studies on Periarteritis Nodosa, II; The Role of Various Factors in the Etiology of Periarteritis Nodosa in Experimental Animals. Smith, C. C., and Zeek, P. M.: Am. J. Path. **23**: 147, 1947.

Typical lesions of periarteritis nodosa occurred in the majority of unilaterally nephrectomized rats, when hypertension was produced by inducing perinephritis in the remaining kidney. The perinephritis resulted from placing either sterile or infected silk suture material around the kidney. These lesions failed to develop under the following experimental conditions which do not elevate the blood pressure: (1) when one kidney was similarly treated but the other was left intact; (2) when the spleen was wrapped in sterile or infected silk; or (3) when the silk or similar infectious agents were introduced into the peritoneal cavity at a distance from the kidney. Lesions of periarteritis nodosa failed to develop in five rabbits sensitized to horse serum. It is suggested that periarteritis nodosa is associated with a sharply rising hypertension. The theory that periarteritis nodosa is the result of hypersensitivity is questioned. J. SHERMAN.

Morphological Equivalents in Polyarthritis Rheumatica, Periarteritis Nodosa, Transient Eosinophilic Infiltration of the Lung and Other Allergic Syndromes. Bergstrand, H.: J. Path. and Bact. **58**: 399, 1946.

Four patients, ranging in age from 17 to 43 years, three of whom were females, died after illnesses which had lasted from six weeks to over three years. They had manifested asthma, blood eosinophilia, severe diarrhea, hemoptysis, and pleurisy. One patient had joint pains. Autopsies revealed lesions typical of periarteritis nodosa in many organs, and polyarthritis rheumatica. Changes in the lungs very similar to those described by von Meyenberg as characteristic of acute transient lung infiltration and changes closely resembling those described for cases of rheumatic pneumonia ("Fruhinfiltrat" and rheumatic granulomas) were found. It is suggested that the etiologic allergic factor may be either "intrinsic" or "extrinsic." E. KAILIN.

Complement Fixation and Precipitin Tests in Trichinosis. Frisch, A. W., Whims, C. B., and Oppenheim, J. M.: Am. J. Clin. Path. **17**: 24, 1947.

More than 200 sera from patients with mild clinical trichinosis were subjected to complement fixation tests at the onset of the disease, and three, six and twelve weeks later. The maximal incidence of fixation occurred three weeks from the onset of symptoms and was found in 37 per cent of the sera tested at this time. Interface precipitation occurred in 6 per cent of the sera, but these "precipitin reactions" were neither "reliable nor reduplicable." E. KAILIN.

Immunologic Reactions in Trichinosis With Purified Antigens. Frisch, A. W., Whims, C. B., and Oppenheim, J. M.: Am. J. Clin. Path. **17**: 29, 1947.

Intracutaneous tests were performed on a group of 112 persons who had contracted trichinosis during an epidemic. A 1:10,000 alkaline-saline extract, an acid-soluble protein preparation and a polysaccharide preparation were made from Trichinella spiralis. The cutaneous reactivity of the polysaccharide preparation was almost inert and the acid-soluble protein preparation was distinctly less reactive than the crude saline extract. Boiling the saline extract did not diminish its cutaneous reactivity. Complement fixation tests indicated that the acid-soluble protein antigen was as reactive as the saline extracts. The antigen active in complement fixation was precipitable by acetone and by alcohol. E. KAILIN.

Intradermal Reactions in Trichinosis. Frisch, A. W., Whims, C. B., and Oppenheim, J. M.: Am. J. Clin. Path. **17**: 16, 1947.

During an epidemic of mild trichinosis among 250 German prisoners of war, intracutaneous tests were performed on the victims with a 1:10,000 dilution of trichina extract. The tests were made at the time the clinical diagnosis was established and were repeated on the same individuals three, six, and twelve weeks later. Varying results were obtained with five trichina antigen preparations. Immediate or delayed reactions were considered positive when they exceeded a diameter of eight millimeters. Approximately half of the infested group showed immediate positive reactions during the period of observation and a slightly greater proportion manifested delayed reactions. E. KAILIN.

Histamine Antagonists. IV: Pyridil-N'Benzyl-N-Dimethylethylenediamine (Pyribenzamine) in Symptomatic Treatment of Allergic Manifestations. Feinberg, S., and Friedlaender, S.: Am. J. M. Sc. **213**: 58, 1947.

Pyribenzamine was found to be an effective palliative drug in the treatment of urticaria, angioneurotic edema, hay fever, vasomotor rhinitis, and serum sickness. It was only moderately effective in the treatment of asthma. The pruritus of atopic dermatitis and of other dermatoses, including pruritus vulvae, was well controlled by the drug. In over 300 cases treated in this series, side-effects were frequently encountered but were usually mild in character. F.

Anaphylaxis

The Rapid Production of Acute Disseminated Encephalomyelitis in Rhesus Monkeys by Injection of Heterologous and Homologous Brain Tissue With Adjuvants. Kabat, E. A., Wolf, A., and Bezer, A. E.: J. Exper. Med. **85**: 117, 1947.

When nineteen Rhesus monkeys received three intramuscular injections of an emulsion of rabbit or monkey brain and adjuvants, all but two became ill and showed lesions of the central nervous system resembling acute disseminated encephalomyelitis observed in human beings. Monkeys receiving emulsions of adult rabbit lung or fetal rabbit brain and adjuvants failed to show similar lesions. Histologically, the lesions were primarily vascular and most commonly involved the white matter of the cerebrum. Early lesions showed congested and edematous vessels with perivascular infiltration of neutrophiles and myelin degeneration of neighboring fibers. In older lesions, lymphocytes and epithelioid lymphocytes replaced the neutrophiles and there was an asso-

ciated perivascular microglial proliferation. It is suggested that antibodies to the injected brain emulsion react with the tissues of the nervous system of the monkey to produce the pathologic changes. E. WALZER.

Allergic Encephalomyelitis in Response to Injection of Normal Monkey Nervous Tissue. Morgan, I. M.: J. Exper. Med. **85**: 131, 1947.

Rhesus monkeys received a series of subcutaneous injections consisting of a mixture of adjuvants and homologous cerebral gray matter, white matter of the corpus callosum and internal capsule, normal spinal cord, poliomyelitic-infected cord, kidney, or peripheral nerves. Within from two to seven weeks, a majority of animals that received cerebral white matter, normal and polioencephalitic cords, and a few animals that had received cerebral gray matter, developed signs of encephalomyelitis. At autopsy, hemorrhages of various sizes were noted primarily in the cerebral white matter and occasionally in the cord. Histologically, the lesions which were confined to the central nervous system consisted of perivascular and extravascular infiltrations of mononuclear cells and polymorphonuclear leucocytes including many eosinophiles. Myelin degeneration was found at the periphery of areas of intense reaction. The encephalitis probably resulted from isoimmunization to central nervous system tissue, particularly to white matter. The encephalopathy observed in a few monkeys injected with gray matter might have resulted from contamination of the injectant with 10 per cent white matter. E. WALZER.

The Relationship of Sulfhydryl and Disulfide Groups to the Antigenic Power of Bovine Serum Albumin. Williams, R. R.: J. Immunol. **55**: 161, 1947.

The sulfhydryl and disulfide radicals of normal bovine serum albumin were chemically altered by various methods. The altered serum albumin in each instance contained little or none of these groups as determined by qualitative chemical tests. With the change in these chemical groups, the serum albumin lost its antigenic power as measured by its capacity to produce anaphylaxis in guinea pigs. It appears that the antigenicity of bovine serum albumin depends on its content of sulfhydryl and disulfide radicals. Further investigation is needed to determine whether this relationship holds true for other proteins. J. SHERMAN.

The Relationship of Acquired Resistance, Allergic Anti-Bodies and Tissue Reactivities to the Components of the Tubercle Bacillus. Raffel, S.: Am. Rev. Tuberc. **54**: 564, 1946.

The typical tuberculin reaction, previously elicited only with whole tubercle bacilli, was induced in guinea pigs by the injection of a purified wax fraction of the tubercle bacillus. Defatted bacilli failed to induce cutaneous sensitivity to tuberculin. Animals sensitized to the wax fraction were not anaphylactically sensitive to Old Tuberculin, but did show an accelerated local reaction to infection with tubercle bacilli. Uninjected controls and animals vaccinated with defatted bacilli showed no evidence of allergic response to the same infecting dose. This is the first instance in which allergy to tuberculosis has been induced separately from immunity. Attempts to transfer passively the tuberculin sensitivity by injecting normal animals with the sera of wax fraction sensitized animals were unsuccessful. Antibodies were found for high molecular weight bacillary protein, for acid-fast wax, crude and purified phosphatide, and, in one instance, for polysaccharide. However, the presence of antibodies to these fractions could not be correlated with resistance to tuber-

culous infection. It is suggested that the particular component of the tubercle bacillus responsible for inducing acquired immunity may lie in one of the minor, as yet untested, fractions of the cell. E. KAILIN.

Pharmacodynamic Studies of a New Antihistaminic Agent, Pyribenzamine (N, N-Dimethyl-N′Benzyl-N′ (alpha Pyridyl)-Ethylene Diamine Hydrochloride). II. Effects on Smooth Muscle of the Guinea Pig and Dog Lung. Yonkman, F. F., Oppenheimer, E., Rennick, B., and Pellet, E.: J. Pharmacol. and Exper. Therap. **89**: 31, 1947.

In vitro experiments with isolated, perfused guinea pig lungs showed that pyribenzamine effectively antagonized histamine-induced bronchial constriction. Antergan afforded similar protection. Horse serum caused immediate, marked, sustained bronchiolar contraction in lungs of guinea pigs sensitized to horse serum. Pyribenzamine added to the perfusate did not counteract a subsequently induced horse serum contraction. Pyribenzamine was administered to seven horse-serum-sensitized guinea pigs in a dosage of 20 mg. per kilogram, twenty minutes before excision of the lungs. This dose was sufficient to cause the toxic reactions of tremors, gasping, and incoordinated locomotion. The subsequent bronchiolar reaction to horse serum was lessened in three and unaffected in four of these animals. This lack of protection in anaphylaxis as contrasted to protection from histamine-induced bronchiolar constriction is discussed.

Dog lungs in situ responded variably to histamine. Histamine-induced bronchiolar constriction could be completely counteracted by pyribenzamine (usually 3 mg. per kilogram). The hypotension resulting from histamine was also combatted to some extent. The vascular anaphylactic reaction of horse-serum-sensitized dogs could be prevented by pyribenzamine in 3.5 mg. dosage. "In none of ten experiments with horse-serum sensitized dogs were we able to demonstrate any contraction of the bronchial musculature after administration of horse serum . . . although anaphylaxis was evident. . . ." It is suggested that factors other than histamine might play a role in anaphylaxis in the dog. Pyribenzamine had little effect on acetylcholine or mecholyl-induced histamine-like reactions. E. KAILIN.

Histamine Antagonists VI.: Comparative Antihistaminic Activity of Some Ethylenediamine Drugs in the Guinea Pig. Friedlaender, S., Feinberg, S. M., and Feinberg, A. R.: J. Lab. and Clin. Med. **32**: 47, 1947.

Benadryl, antergan, pyribenzamine, and neoantergan were administered to guinea pigs in doses of 3 mg. per kilogram fifteen minutes prior to the intravenous injection of a toxic dose of histamine. Histamine in a dose of 0.4 mg. per kilogram fatally shocked 100 per cent of unprotected control animals. The mortality of benadryl-protected animals was 29 per cent among guinea pigs given the 0.4 mg. dose of histamine. A mortality of 100 per cent was attained in benadryl-protected pigs when a dose of 2 mg. of histamine per kilogram was given. Antergan afforded a similar degree of protection. Pyribenzamine protected most animals against 10 mg. of histamine per kilogram, while a dose of 15 mg. was necessary to kill all animals in the pyribenzamine-protected group. Neoantergan protected more than half the pigs from 25 mg. per kilogram of histamine, while 50 mg. was the dose required to give 100 per cent mortality in this group of animals. These drugs were also found to be capable of modifying anaphylaxis in the guinea pig. Preliminary studies failed to show wide variations in the antianaphylactic activity of these four drugs comparable to their effect on histamine shock.
E. KAILIN.

Pyribenzamine Aerosol Inhalation and Its Influence on Histamine Poisoning and Anaphylaxis. Mayer, R., Brousseau, D., and Eisman, P. C.: Proc. Soc. Exper. Biol. and Med. **64**: 92, 1947.

Guinea pigs exposed to pyribenzamine as a 2 per cent aerosol were protected against 15 lethal doses of histamine injected intracardially. The protection afforded depended upon the duration of the inhalation. Animals so protected and injected with histamine became deeply narcotized for from thirty to sixty minutes and exhibited regular, slow, superficial respirations, with occasional athetotic movements of all extremities. The protection afforded by pyribenzamine aerosol in actively sensitized guinea pigs was less regular than that in the histamine series. Although all actively sensitized animals could be protected against immediate shock and anaphylactic death, some animals died within the ensuing twenty-four hours. Passively sensitized guinea pigs were better protected than actively sensitized animals. Trasentine or procaine aerosol failed to protect animals against poisoning. Pyribenzamine did not produce any clinical symptoms of irritation or pathological changes in the lungs exposed to the aerosol for one or two hours. It is concluded that the action of pyribenzamine in counteracting histamine is peripheral. The drug is either selectively fixed within the receptor cells of the lung or, by direct contact, renders the cell refractory to histamine. The therapeutic use of pyribenzamine as an aerosol is suggested. E. WALZER.

Miscellaneous

Further Experimental Studies on the Role of the Plasma Cells as Antibody Producers. Bjørneboe, M., Gormsen, H., and Lundquist, Fr.: J. Immunol. **55**: 121, 1947.

Rabbits were immunized by the intravenous administration of a vaccine containing eight types of pneumococci every other day for periods ranging from one to eight months. The animals were then exsanguinated. The lungs, liver, kidneys, muscle thymus, lymph nodes, retroperitoneal and renal pelvis fat were examined histologically. Extracts of these tissues were analyzed for antibody content. The adipose tissue of the renal pelvis showed a slight lymphocytic infiltration (10 per cent) and a massive plasma cell proliferation (90 per cent). Fewer plasma cells were present in the other organs examined. The antibody content of renal sinus adipose tissue was considerably greater than that of the other organs assayed. These findings suggest that antibodies are produced by plasma cells. E. WALZER.

Eosinophilic Granuloma of the Bone. Report of a Case With Multiple Lesions of Bone and Pulmonary Infiltration. Weinstein, A., Francis, H. C., and Sprofkin, B. F.: Arch. Int. Med. **79**: 176, 1947.

A 31-year-old man complaining of intermittent headache and backache and a nonproductive cough showed roentgenologic evidence of bony defects in the skull, ilium, pubis and body of the third vertebra. Physical and laboratory examinations were essentially negative except for some tenderness on deep palpation over a small area in the left parietal bone and a mild but persistent eosinophilia. X-ray of the chest revealed a fine nodular type of infiltration in the upper halves of both lung fields. Biopsy of a skull lesion revealed the presence of many focal accumulations of eosinophiles. The patient was given x-ray therapy to the involved areas and within a few months showed evidences of healing in certain of the sites. Two years later, x-ray examina-

tion showed definite improvement in all of the lesions except the curretted skull area. It is believed that the pulmonary lesions were a visceral involvement as part of the general picture of eosinophilic granuloma of the bone. F.

Acute and Chronic Toxicity Studies on Theophylline Aminoisobutanol and Theophylline Ethylenediamine. Thompson, C. R., and Warren, M. R.: J. Lab. and Clin. Med. **31**: 1337, 1946.

Studies on acute intravenous toxicity were carried out in rabbits and on oral toxicity in mice. In rabbits, the intravenous LD_{50} of theophylline aminoisobutanol was 163 mg. per kilogram and that of theophylline ethylenediamine was 150 mg. In mice, the oral $LD's_{50}$ were 600 and 540 mg. per kilogram respectively. Death was preceded by convulsions and usually occurred within ninety minutes, but sometimes was delayed for several days. Dogs received these two drugs orally or intravenously in doses of 20 mg. per kilogram six days weekly for twelve weeks and showed no hematologic or histologic evidence of toxicity. Rats given up to 34 mg. per kilogram orally every day for as long as sixty days likewise failed to show evidence of toxic reaction. E. KAILIN.

Effect of Antihistamine Drugs on Increased Capillary Permeability Following Intradermal Injections of Histamine, Horse Serum, and Other Agents in Rabbits. Last, M. R., and Loew, E. R.: J. Pharmacol. and Exper. Therap. **89**: 81, 1947.

Trypan blue, injected intravenously into albino rabbits, was used to detect changes in capillary permeability produced by the intracutaneous injection of 0.02 ml. of minimally effective concentrations of histamine, horse serum, trypsin, snake venom, staphylococcus toxin, heparin, codein, and tetracaine. Benadryl and neoantergan (2786 R P) blocked capillary permeability induced by histamine in concentrations below 0.5 mg. per ml. Benadryl failed to affect the spread of trypan blue induced by the other agents, indicating that the increased permeability caused by them is not mediated by histamine. Sensitized rabbits were injected intracutaneously with serial dilutions of horse serum. Benadryl administered thirty minutes prior to testing "failed to induce either qualitative or quantitative differences in reactions" resulting from horse serum in dilutions of 1:1,000 or less. The response to a 1:5,000 dilution of horse serum was somewhat diminished in the Benadryl treated animals. With higher dilutions of horse serum the incidence of trypan blue reactions was very low in both treated and untreated animals. Since mecholyl failed to induce a positive trypan blue reaction in most animals, it appeared unlikely that choline or a choline ester is involved in the changes in capillary permeability observed. The significance of the failure of benadryl to counteract the horse serum antigen-antibody reaction in rabbit skin is discussed. E. KAILIN.

Influenza Vaccination: Comparison of Intracutaneous and Subcutaneous Methods. Van Gelder, D. W., Greenspan, F. S., and Dufresne, N. E.: U. S. Nav. M. Bull. **47**: 197, 1947.

The immune response induced in individuals with small intracutaneous doses of influenza virus vaccine was compared with the response induced by the subcutaneous innoculation of large doses. One group of subjects received a single dose of 0.1 c.c. of the vaccine intracutaneously; the second group received two such doses two weeks apart; the third group received one dose of 1.0 c.c. subcutaneously; the fourth group received one dose of 0.1 c.c. of control material. The incidence of both local and general reactions was lower when the vaccine was administered intracutaneously. The greatest rise in

titre against both influenza virus A and B was observed in the group which received a single dose of 0.1 c.c. vaccine intracutaneously. The degree of protection afforded against influenza by the intracutaneous injection of the vaccine has not been determined clinically. J. SHERMAN.

The Effect of Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) Upon Permeability of Meningeal Capillaries. Gelvin, E. P., Elias, H., and McGavack, T. H.: J. Pharmacol. and Exper. Therap. **89**: 101, 1947.

Dogs chronically intoxicated with benadryl manifest congestion of the choroid plexus. The permeability of the meningeal capillaries of five neurologic patients was measured by the intravenous injection of fluorescein, the spinal tap being performed one hour later. The patients were then given 300 to 450 mg. of benadryl daily for one week after which the fluorescein permeability test was repeated. No change in capillary permeability was found. Central nervous system disturbances caused by the benadryl were not accompanied by alteration in cerebrospinal fluid sugar, protein, chloride, cellular composition, colloidal gold or Wassermann reactions. The concentration of benadryl in the cerebrospinal fluid was similar to that in the blood. E. KAILIN.

The Nature of Benadryl Activity: Glucose Tolerance Curves. Reinstein, H., and McGavack, T. H.: J. Clin. Endocrinol. **6**: 643, 1946.

The effect of benadryl on the glucose tolerance curves of fourteen nondiabetic, convalescent patients was studied. Benadryl was always administered one-half hour before the test was started. When the drug was taken in a single, oral dose of 400 mg., no effect on the glucose tolerance was noted. When 30 mg. of benadryl were administered intravenously, there was an increase in glucose tolerance. It is suggested that the action of benadryl is mediated through the liver. E. WALZER.

An Attempt to Prevent Histamine-Induced Ulcers in Guinea Pigs With Benadryl. Crane, J. T., Lindsay, S., and Dailey, M. E.: Am. J. Digest. Dis. **12**: 56, 1947.

The incidence of histamine-induced gastric and duodenal ulcers in guinea pigs did not appear to be affected by the intraperitoneal administration of benadryl in daily doses of 135 mg. per kilogram of body weight. F.

Prolonged Reaction to Benadryl. Schwartzberg, S., and Willerson, D.: J. A. M. A. **133**: 393, 1947.

Benadryl, taken in 50 mg. doses two to three times a day by a 38-year-old white man, for relief of hay fever, caused moderate drowsiness during the first week of its use. During the second week, the patient noted puffiness of the eyes and an increased number of bowel movements. In the third week, a feeling of tightness in the arms, forearms, hands and behind the knees developed; together with numbness and tingling of the hands, drowsiness and mental sluggishness. The drug was then discontinued. Slow improvement in the symptoms followed until, after three months, there remained only slight discomfort beneath the right antecubital fossa under conditions of strain. Most of the above complaints appeared to be an intensification of some of the usual side effects of benadryl. Neuritic symptoms have been produced in dogs by the intravenous injection of benadryl. F.

Allergy Abstracts

Asthma and Hay Fever

Asthma in Children. Treatment With the Radium Nasopharyngeal Applicator. Ward, A. T., Jr., Livingston, S., and Moffat, D. A.: J. A. M. A. **133**: 1060, 1947.

Thirty-four asthmatic children ranging in age from 2 to 14 years who had lymphoid hyperplasia in the nasopharynx were treated with the radon nasopharyngeal applicator. All the children in the group were thoroughly investigated from the otolaryngologic, allergic, and pediatric points of view. The majority of the group had had asthmatic symptoms for two or more years prior to the irradiation treatment. Sixteen had had previous tonsillectomies. The thirty-four cases included intrinsic and extrinsic types of asthma, as well as mixed or unclassified types. Eighty per cent of the entire group developed asthmatic attacks after every respiratory infection regardless of the specific causes involved. Treatment consisted of the application of 2 Gm. minutes of radon to each side of the nasopharynx once each month for an average of four treatments. At the end of this therapeutic regime, there was complete disappearance of the lymphoid tissue in twenty-three of the thirty-four cases. Fifteen patients were completely relieved of asthmatic attacks, five others had only mild attacks, and three showed diminution in the number and severity of the attacks. Improvement was ascribed to the reduction in the lymphoid tissue with resulting diminution in the number of infections. The type of asthma had no apparent bearing on the success of the therapy, and the improvement following irradiation could not be credited to removal of extrinsic factors, since elimination of such offending agents prior to irradiation had not affected the asthma. Other factors resulting from the radon treatment, such as reduction in postnasal secretion, change in bacterial flora, and change in the threshold of absorption of allergens from the nasopharynx, probably played a role in the relief of these children. F.

Hay Fever Plants of Albuquerque, New Mexico. A Preliminary Report. Werner, W. I., Reed, W. G., and Stormfels, E. E.: Ann. Allergy **5**: 47, 1947.

A pollen survey of Albuquerque, New Mexico, was conducted in 1945. Four stations were set up from four to forty feet above ground level. The gravity method of collecting pollen was employed. The daily pollen counts were expressed as the number of grains per square centimeter of glycerine-jelly-covered slide for a 24-hour exposure. The counts were reported as the average of the four stations and were correlated with frequent field trips. It was found that the major hay fever period extended from April 13 to October 28. The spring season from February 12 to May 7 produced the highest counts, with juniper, cottonwood, and Bermuda grass as the prime offenders. Severe symptoms were

noted on April 13 and were apparently due to cottonwood. The summer season extended from May 7 to August 7 with Bermuda grass, Russian thistle, and plantain in profusion. Russian thistle, pigweed, and false ragweed were the chief offenders during the fall season which extended to the first week of November. Counts for the spring season ranged as high as 1,400; during the summer and fall season, they were generally below 100. E. WALZER.

Chemical, Physical and Immunological Properties of Electrophoretically Purified Pollen Extracts. Abramson, H. A.: Ann. Allergy **5**: 19, 1947.

By means of the Tiselius moving-boundary method of electrophoresis, the ultracentrifuge, and precision diffusion devices, it has been possible to isolate and study the properties of Trifidin, Artefolin, and Pratensin, the main colorless constituents of giant ragweed, and timothy pollen, respectively. Pigmented fractions of these inhalants have also been isolated. The evidence presented indicates that Trifidin and Artefolin have a molecular weight of 5,000, and that they are high-molecular-weight polypeptides coupled with other molecules. The colorless as well as the pigmented constituents give positive skin reactions directly and by passive transfer. It is suggested that the allergenic activity of a pollen extract be measured by its immunologic response in preference to chemical standardization procedures. E. WALZER.

Fifteen Years Experience With Carbon Dioxide in the Management of Cough. Banyai, A. L.: Dis. of Chest **13**: 1, 1947.

Cough removes accumulated mucus, exudate, or foreign bodies from the respiratory tract. Pathologic changes in any part of the respiratory tract may provoke cough. Its mechanism and physiology are described. It may be productive and useful or nonproductive and useless. The many causes of nonproductive cough are outlined. Long continued coughing may lead to emphysema. Useless and inadequate cough, referred to as tussic insufficiency, is exhausting and causes stagnation of material within the bronchi, which is a major factor in the pathogenesis of bronchiectasis. The sequelae of prolonged cough may be headache, pulmonary hemorrhage, spontaneous pneumothorax, and fracture of ribs. The management of cough should be directed toward diminishing its frequency and severity, but not at the expense of adequate expectoration. Suppression of the cough reflex by narcotics may be harmful. Some aspects of the physiology of respiration as related to cough are discussed, including the role of the bronchial cilia and bronchial peristalsis. The lung rids itself of secretion and exudate by resorption and expectoration. Carbon dioxide was found to be an efficient expectorant superior to other expectorant drugs. Forty patients with uncontrollable cough and dyspnea were treated with a mixture of CO_2 and O_2, either 10 per cent and 90 per cent, or 5 per cent and 95 per cent, with relief of symptoms. The literature on the use of CO_2 as an expectorant is reviewed. J. SHERMAN.

Bronchial Asthma Caused by Sulfathiazole. Rosberg, M.: Acta med. Scandinav. **126**: 185, 1946.

Two nurses handling powdered sulfathiazole in the course of their daily work developed asthma. Skin tests with sulfathiazole were negative, but positive reactions were obtained in both patients with 2-aminothiazole hydrochloride, and one showed a positive reaction to acetyl sulfanilchloride. These substances may result from the decomposition of sulfathiazole in the body. C.

Contribution to the Study of Respiratory Allergies in Barcelona. Importance of Air Bacteria. Frouchtman, R.: Rev. clín. españ. **23**: 292, 1946.

A mold and bacterial survey of the air in Barcelona showed that Aspergillus, Penicillium, Cladosporium, and Alternaria were the most important molds. Sarcinae and diphtheroids were the dominant bacteria. Bacterial counts increased in the spring and decreased during the summer months. Relatively higher counts were observed in the harbor area of the city. Beneficial results were obtained in twenty-six patients treated with vaccines prepared from these bacteria. In twenty-two of these cases, asthma was completely relieved for periods ranging from several months to more than a year. The aerobacteria are capable of specific action, either in stimulating the appearance or conditioning the chronicity of respiratory allergic diseases. C.

Dermatology

Dermatitis From Contact With Varnish of Japanese Rifles. Cornber, R. B.: Arch. Dermat. & Syph. **55**: 110, 1947.

During the occupation of Japan, numerous instances of dermatitis in members of the armed forces were traced to contact with Japanese rifles which had been confiscated as souvenirs. The lesions were characterized by acute erythema, varying degrees of edema, and vesiculation which involved the hands and forearms and, in some cases, the inner surfaces of the legs and ankles. Positive patch tests were obtained with acetone solutions of varnish scraped from the stocks of several Japanese rifles. Control tests with acetone were negative. Since many thousands of Japanese rifles have been brought back to the United States by returning servicemen, it is suggested that this factor be kept in mind as a possible cause of contact dermatitis. C.

Antipruritic Qualities of Papaverine Hydrochloride. Wirth, F.: J. Invest. Dermat. **8**: 63, 1947.

Twenty-nine patients suffering from pruritus associated with jaundice, dermatitis venenata, trichophytosis, urticaria, et cetera, received one grain of papaverine hydrochloride intravenously for symptomatic relief. All experienced a moderate to complete antipruritic effect which lasted from one to six hours. E. WALZER.

Poison Oak Dermatitis. Studies on Hematologic, Urinary and Temperature Changes. Templeton, N. J., Lunsford, C. J., and Allington, H. V.: J. Invest. Dermat. **8**: 53, 1947.

Of one hundred six patients with severe poison oak dermatitis, eighty-two developed low grade febrile reactions. The temperature rose to above 100° F. in only ten of these cases. A mild leucocytosis was observed in fifty-five patients of whom forty-five showed an eosinophilia ranging up to 15 per cent. Urinalyses in all patients were essentially normal. E. WALZER.

Modifications of the Goldman Technique for Contact Testing of the Buccal Mucosa. Farrington, J.: J. Invest. Dermat. **8**: 59, 1947.

Contact testing of the buccal mucosa may be facilitated in patients with dentures by attaching a small rubber cup containing the contactant to the plate surface adjacent to the mucous membrane by means of collodian. In children, the contact cap, a rolled finger cot, is firmly but comfortably fixed by suturing it to dental floss which is passed between the teeth and anchored to a small button. E. WALZER.

Benadryl in Dermatologic Therapy. Lynch, F. W.: Arch. Dermat. & Syph. **55**: 101, 1947.

Four of ten cases of acute urticaria were relieved within twenty-four hours after the oral administration of 50 mg. of benadryl six times daily. Of twenty-three patients with chronic urticaria, all but two were improved following benadryl therapy. Pruritus was diminished in 60 per cent of five cases of vulvar pruritus and in 60 per cent of eleven cases of insect bites. Results were "inconclusive but somewhat encouraging" in erythema multiforme, rosacea, and lupus erythematosus. Six patients with neurodermatitis, two with contact dermatitis, two with dermatitis herpettiformis, and one with periarteritis nodosa were not relieved by benadryl. C.

Unusual Reaction Following Benadryl Administration. Geiger, J., Rosenfield, S. Z., and Hartman, D. L.: J. A. M. A. **133**: 392, 1947.

A 26-year-old white woman with seborrheic dermatitis was given benadryl to relieve the pruritus. Three 50 mg. doses were administered daily. After a total of 300 mg. had been taken over a period of three days, the patient complained of palpitation, dimmed vision, malaise, drowsiness, heartburn, and nausea. Following the next regular dose of 50 mg., the patient was found unconscious. She was cold, pale, and pulseless; blood pressure readings were not recordable. The pupils were equal and reacted to light. The patient responded to epinephrine. Three hours later she had recovered completely but had no recollection of the preceding events. Seven days following the shock-like reaction treatment with benadryl was resumed. Once more after 300 mg. had been taken over a period of three days, the patient complained of palpitation, severe malaise, dimmed vision, and nausea. She became somewhat disoriented and excited. The drug was discontinued and the patient rapidly returned to normal. F.

The Nature of Halogen Sensitivity in Dermatitis Herpetiformis and Pemphigus. Felsher, Z.: J. Invest. Dermat. **8**: 55, 1947.

When five patients with dermatitis herpetiformis were patch tested on normal skin with 20 per cent potassium iodide and 20 per cent thiocyanate in a petrolatum base, four developed vesicular reactions of equal size to both drugs. Four patients with epidermolysis bullosa and twenty-nine of thirty normal individuals similarly patch tested showed negative reactions. Biopsy of the blisters produced by the potassium iodide showed separation at the epidermal-dermal junction. It is suggested that there is a changed electrolytic state of the collagen in dermatitis herpetiformis and pemphigus and that the iodide and bromide ions cause a further reduction of the adhesiveness of corium to epidermis. This factor explains the formation of bullae when iodides are administered to patients with dermatitis herpetiformis. E. WALZER.

Dermatitis Following Paratoluylenediamine Hair Dye. Lawrence, M. W.: J. Invest. Dermat. **8**: 177, 1947.

Dermatitis followed the use of paratoluylenediamine hair dye. In six cases, the sensitivity was manifested by itching, erythema, swelling, and exudation of the skin, with occasional papules and vesiculation. The lesions were limited to the site of application or to points of contact. In five of the six cases, there had been previous contact with the dye. Patch testing with paratoluylenediamine was not done in every patient and was strongly positive in only one case.

There was no evidence to indicate that the dye was absorbed in the sensitized subjects or in nonsensitive controls who had used the dye repeatedly. E. WALZER.

Studies on the Adherence of the Epidermis to the Corium. Felsher, Z.: J. Invest. Dermat. **8**: 35, 1947.

Studies on the adherence of the epidermis to the corium indicate that connective tissue swells in acid or alkaline solution. The greater the acidity or the alkalinity of the solution in which a specimen of skin is immersed, the more the collegen swells and the more easily can the epidermis be separated from the corium. Alkali also causes the separation of the epidermal cells from each other. Divalent alkalis such as calcium hydroxide cause less swelling of collagen than monovalent alkalis such as sodium hydroxide and thus inhibit separation of the epidermis. Sodium chloride in the presence of acid or base inhibits the swelling of the corium and the separation from the epidermis. Neutral salts, such as thiocyanate, iodide, and bromide, cause rapid swelling of collagen and separation of the epidermis, whereas other neutral salts, such as sulfate, acetate, and citrate, tend to shrink and dehydrate the tissues and thus prevent separation at the epidermal-dermal junction. Following separation of the epidermis from the corium, the process can be reversed and the adherence of the two layers restored by treatment of the skin with salts causing shrinkage of collagen. This adherence is rather temporary and after a day the epidermis again becomes separated. Separation of the epidermis by heat is hastened by salts which cause swelling of collagen, and is retarded by those which shrink it. Separation of the epidermis from the corium in edematous skin may be explained by a change from the colloidal to the sol state which diminishes adhesive and cohesive properties. J. SHERMAN.

A Method for Protection of Patients With Solar Urticaria. Rubin, L., Beal, P. L., and Rothman, S.: J. Invest. Dermat. **8**: 189, 1947.

A sixfold increase in tolerance to light was noted in two patients with solar urticaria during therapy with pyribenzamine. One of the patients was treated with increasing doses of artificial sunshine and diminishing doses of pyribenzamine. Daily irradiations were continued for two weeks after stopping pyribenzamine. Tanned treated areas were found to have a tolerance of more than two hundred times that of covered parts. The effect of ultraviolet irradiations is regarded as "local and due to pigmentation and/or thickening of the horny layer whereby the penetration of antigenic wavelengths is inhibited."

E. WALZER.

Eczema and Essential Fatty Acids. Hansen, A. E., Knott, E. M., Wiese, H. F., Shaperman, E., and McQuarrie, I.: Am. J. Dis. Child. **73**: 1, 1947.

The average iodine number of the serum fatty acids in 171 eczematous patients of various age groups was lower than the average number of 101 control subjects, indicating a low level of unsaturated fatty acids in this condition. When fats, such as lard, which are rich in unsaturated fatty acids, were fed to 148 of the eczematous patients, the clinical response was good in sixty, fair in fifty-one, and poor in thirty-seven. The best results occurred in young patients with 88 per cent of infants, 64 per cent of children, and 60 per cent of adults showing improvement. The iodine number rose in the improved patients indicating an increase in the unsaturated serum fatty acids, which paralleled the degree of clinical improvement. Patients treated only with applications of crude coal tar ointment who improved clinically also showed a rise in the iodine

number. The role of unsaturated fatty acids seems to be that of maintaining normal skin metabolism. In addition to elimination of known food offenders, and local therapy with tar, it is suggested that eczematous patients be given a diet including an adequate amount of fats rich in unsaturated fatty acids.

J. SHERMAN.

Pyribenzamine in Experimental Nonallergic and Allergic Dermatitis. Mayer, R. L.: J. Invest. Dermat. **8**: 67, 1947.

Pyribenzamine was injected subcutaneously in doses of 10 or more mg./kg. fifteen minutes prior to the application of 10 per cent mustard oil in vaseline to the skin of guinea pigs. The appearance of the irritation was retarded up to forty minutes and the intensity of the reaction was diminished for the next thirty to sixty minutes. A dose of 20 mg./kg. of pyribenzamine diminished the immediate irritation and urticarial reaction which usually developed when turpentine in 50 to 70 per cent concentrations in sesame oil was applied to the skin of rabbits. However, within twenty-four hours, dermatitis was present in variable degree in all pyribenzamine-treated animals. P-phenylendiamine-sensitized guinea pigs, treated with pyribenzamine before, during, or after the challenging application of the contactant, responded with a dermatitic reaction in which the inflammation and discoloration were weaker than in control animals. When pyribenzamine in 5 per cent solution was applied locally during and following the challenging dose, the protection afforded was greater than in animals in which the drug was administered parenterally. It is concluded that histamine plays an active role in the initial phase of skin irritation as well as in the development of contact dermatitis. It is suggested that the dosage of pyribenzamine required for the effective treatment of epidermal allergy (contact dermatitis) is greater than that for allergy of other systems.

E. WALZER.

Otorhinology and Ophthalmology

Vasomotor Rhinitis Medicamentosa Viewed Histologically. Ryan, R. E.: Proc. Staff Meet. Mayo Clin. **22**: 113, 1947.

Histologic changes in the nasal membranes of rabbits were studied following excessive instillation of nose drops. Two types of nose drops (dl-desoxyephedrine with sodium sulfathiazole and sodium sulfadiazine with naphazoline hydrochloride) were applied by the dropper method five times a day to the nasal membranes of a series of rabbits. At various intervals, specimens of mucous membrane were removed, sectioned and compared with sections of normal rabbit membrane. The cilia were found to have been destroyed after five or eight days' use of both types of nose drops. The blood vessels were dilated in the early stages, but, by the fortieth day, they were constricted or even sclerosed. Inflammatory cells were evident in the early stages but disappeared after the fourth week. Epithelial cells became damaged as early as the fifth day and during the second week showed signs of edema and degenerative changes. Finally, the epithelial cells underwent metaplasia from ciliated columnar epithelium to nonciliated stratified squamous epithelium and fibrosis of the subepithelial layer of the nasal mucous membrane developed. C.

Effect of Emotions on the Hydrogen Ion Concentration of Nasal Secretion in Situ. Fabricant, N. D.: Arch. Otolaryng. **43**: 402, 1947.

There is a definite relationship between emotional factors, the frequency of colds and altered nasal function. Congestion of the nasal mucous mem-

brane may occur as an accompaniment of anxiety or resentment. Nasal PH varies with sleep and rest, diurnally and nocturnally and with the ingestion of food. Emotional upsets and fright deliberately induced in three subjects during the determination of their nasal PH, resulted in a rapid shift in PH from slightly acid (6.50) to alkaline (7.33). After four or five minutes the PH returned to its original acid state. It is only in susceptible persons that emotional changes can produce transient conversions of nasal secretion from a normal slightly acid to an abnormal alkaline state. C.

Absence or Near Absence of Excitant Effects From Administration of Tuamine. Boyd, E. M., Copeland, J., and Lapp, F. H.: Arch. Otolaryng. **44**: 166, 1946.

Among the disadvantages of inhalers used in local therapy of the nasal congestion of allergic rhinitis and allied conditions is the cerebral excitement which they produce when used excessively. Experiments with Tuamine on 2,000 animals including white mice, albino rats, guinea pigs, rabbits, and cats failed to show any evidence of cerebral excitation in most of the anesthetized animals. The activity of unanesthetized albino rats, as registered in activity wheels, was not increased by injections of Tuamine sulfate in doses up to one-fifth the LD_{50} dose. It is concluded that Tuamine in therapeutic doses, and even in doses somewhat above the therapeutic level, has little or no excitant effect on the central nervous system. C.

A Diagnostic Test for Allergic Reactions in Maxillary Sinuses. Frouchtman, R., and Ferrando, J. M.: Rev. clín. Espan. **22**: 219, 1946.

The subcutaneous injection of one-half to one cubic centimeter of adrenalin 1:1,000 in eight patients with allergic sinusitis resulted in a lessening of the opacity of the maxillary sinuses as demonstrated by x-ray. Apparently the opacity was due to an edema of the sinus mucosa and this edema was reversible. In chronic allergic sinusitis where fibrotic changes have taken place in the mucosa, adrenalin will reduce mucosal edema but will not clear up sinus opacity. This procedure is offered as a new diagnostic test to determine whether the opacity is due to chronic infection or allergic edema. C.

Miscellaneous Allergies

Fatal Allergic Reactions Due to Influenza Vaccine. Curphy, T. J.: J. A. M. A. **133**: 1062, 1947.

Stock influenza type A. and B. vaccine was administered to five members of a family, one of whom was a 3-year-old girl. The family history was negative for allergy. The child had had one attack of hives following the ingestion of aspirin. There was no history of egg sensitivity. Four hours after the administration of 0.5 ml. of the vaccine, she began to have pain in the abdomen, chills, vomiting and convulsions. When the rectal temperature rose to 109° F., she was removed to a hospital. Cyanosis, a pulse rate of 180 per minute, and moist rales over both pulmonary fields were noted. The symptoms increased in severity, despite the administration of oxygen and epinephrine. Bleeding occurred from the vagina, the mouth and at the sites of hypodermic injections. Cheyne-Stokes breathing developed and convulsions occurred at one or two-minute intervals. Profound shock and circulatory collapse occurred seven hours after the onset of the reaction and death ensued. Postmortem examination revealed widespread hemorrhages, air emboli, and early interstitial pneumonia suggestive of a virus infection. The virus pneumonia may have been the sensitizing factor which

accounted for the high degree of reactivity in this patient. The hemorrhagic reaction was compared to a Shwartzman phenomenon. On the basis of the clinical picture, the author maintains that this is a case of pronounced sensitivity to the influenza vaccine, although necropsy findings were not characteristic of typical anaphylactic shock. F.

Anaphylacitc Shock in Egg-Sensitive Individuals Following Vaccination With Typhus Vaccine. Hampton, S. F.: J. Lab. & Clin. Med. **32**: 109, 1947.

Two instances of immediate, severe, but nonfatal constitutional reactions to the injection of typhus vaccine are reported. Cholera vaccine had been administered at the same time as the typhus vaccine. Each of the two patients had a clinical history of egg intolerance. Reagins for egg white, egg yolk, chicken, and typhus vaccine were demonstrable by passive transfer. Sensitized sites did not react to cholera vaccine. K.

Granulocytopenia Due Probably to "Pyribenzamine." Wyndaham, B. B., and Owens, M. E. B., Jr.: J. A. M. A. **134**: 454, 1947.

A 74-year-old female developed fever and marked depression of granulocytes in the peripheral blood after eight weeks of moderate doses of pyribenzamine. Withdrawal of the drug and administration of penicillin resulted in recovery. The white cell count had dropped from 8,600 with 55 per cent neutrophiles to 1,300 with 3 per cent neutrophiles. F.

Chronic Eosinophilia: Report of a Case With Necrosis of the Liver, Pulmonary Infiltrations, Anemia, and Ascaris Infestation. Perlingiero, J. G., and György, P.: Am. J. Dis. Child. **73**: 34, 1947.

A 2-year-old Negro boy with a past history of "asthmatic bronchitis," and of eczema in infancy developed a septic fever which lasted for several months and was accompanied by severe anemia, leucocytosis, and a persistent eosinophilia up to 84 per cent. There was x-ray evidence of pulmonary infiltration. The liver was enlarged and a biopsy showed a focal necrosis. In the differential diagnosis, Loeffler's syndrome, eosinophilic leucemia, familial eosinophilia, trichinosis, chronic brucellosis, and tuberculosis were considered. When the child vomited and brought up an adult ascaris worm, a rapid recovery followed. Eight months later, the only abnormal finding was a persistent eosinophilia of 34 per cent. J. SHERMAN.

The Treatment of Serum Sickness With Benadryl. Peterson, J. C., and Bishop, L. K.: J. A. M. A. **133**: 1277, 1947.

Ten children who had developed serum sickness following serotherapy were successfully treated with benadryl. Repeated oral doses of benadryl as high as 8 mg. per pound of body weight were well tolerated by small infants. Nausea, which occurred most frequently with the elixir, was observed in several cases but was severe in only one instance. Doses of 50 mg. every six to eight hours were not always effective even in very young infants and larger doses up to 100 mg. every six hours were often required to control the symptoms. Doses of 100 mg. always abolished the symptoms within from two to three hours. For effective results the drug had to be given for the duration of the serum sickness, since the action of benadryl is only suppressive. The effective action of benadryl lasts from six to twelve hours and seems to have a cumulative effect if given oftener than every eight hours. F.

Antergan in the Treatment of Allergic Syndromes. Frouchtman, R.: Med. Clin. **7**: 385, 1946.

The oral administration of antergan in daily doses of 0.40 to 0.60 Gm. for three to six days resulted in improvement in four out of eighteen patients with allergic disease. Of those benefited, two suffered from urticaria, and two had allergic rhinitis. Beneficial results were not obtained in two cases of asthma, one of migraine, eight of urticaria, and three of allergic rhinitis. Most of the patients experienced undesirable side-effects such as anorexia, nausea, pyrosis, insomnia, and vomiting. There was no relationship between the results obtained and skin sensitivity to histamine. Antergan cannot be considered as an anti-allergic panacea. C.

The Effect of Antihistamine Drugs Upon Serum-Induced Myocarditis in Rabbits. Kyser, F. A., McCarter, J. C., and Stengle, J.: J. Lab. & Clin. Med. **32**: 379, 1947.

Sterile, unpreserved horse serum injected into rabbits resulted in lesions very similar to those of acute rheumatic carditis. Of twelve rabbits given serum alone, eleven developed extensive lesions. Nine rabbits were given serum plus 2 mg. benadryl twice daily. Of these animals, four exhibited no lesions, two showed moderate lesions, and three animals which died were not examined. Six rabbits were given serum and 10 mg. per kilogram of benadryl twice daily. Of these, three failed to develop lesions, two showed occasional perivascular infiltrations and one animal had moderate lesions. Serum with a small amount of preservative added induced marked lesions in two rabbits and very slight lesions in a third. Of nine animals which were given this serum with the preservative and an antihistaminic drug designated as "No. 1627," eight either were free of myocardial changes or had very slight infiltrations, while one animal showed moderate changes. There was no Aschoff body type of lesion in the protected animals. It is concluded that the administration of Benadryl circumvents the formation of horse-serum-induced rheumatic carditis-like lesions. K.

Pulmonary Calcifications and Sensitivity to Histoplasmin in Charleston, S. C. Waring, J. I., and Gregg, D. B.: Am. J. Dis. Child. **73**: 139, 1947.

A roentgenographic survey of 494 school children in Charleston, S. C., revealed pulmonary calcification in seventeen. Of these, eight reacted negatively to patch tests with tuberculin. When the negative reactors to tuberculin were tested with 0.1 mg. old tuberculin and a 1:100 dilution of histoplasmin, three reacted negatively and one reacted positively to both antigens, while four reacted positively to histoplasmin only. All five children with positive histoplasmin tests had spent some time in the Mississippi Valley in areas known to have a high incidence of positive reactions to histoplasmin. Among 121 children in an orphan asylum in Charleston, less than 2 per cent showed positive reactions to histoplasmin. E. WALZER.

Anaphylaxis

Effects of Benadryl on Anaphylactic and Histaminic Shock in Rabbits and Guinea Pigs. Campbell, B., Baronofsky, I. D., and Good, R. A.: Proc. Soc. Exper. Biol. & Med. **64**: 281, 1947.

Benadryl protected rabbits against histamine shock, but did not protect against anaphylactic shock in animals actively sensitized to egg white. Similarly, three out of five guinea pigs actively sensitized to egg white by the intraperitoneal route were not protected by benadryl when a shocking dose of antigen was

administered by the same route. These experiments seem to indicate that a substance other than histamine is responsible for anaphylaxis. J. SHERMAN.

Hypersensitivity to Egg White in the Rat. Léger, J., Masson, G., and Prado, J. L.: Proc. Soc. Exper. Biol. & Med. **64**: 366, 1947.

After intraperitoneal injection of egg white in rats, maximal hyperemia of the nose and ears occurred in about two hours. This was followed by edema of the face, tongue, and paws. The response was limited to these areas. The larger the dose, the greater was the intensity of the reaction. The same response occurred within a few minutes after intravenous injection and was maximal after ten to thirty minutes. The injection of large doses of horse serum was without effect. Repeated daily intraperitoneal injections of egg white produced variable results; the degree of edema varied from day to day in the same animal, and the response did not disappear after repeated injections. The age of the animals did not seem to be a significant factor, but female rats tended to be less responsive than males. J. SHERMAN.

A Comparison of the Bronchodilator Activity of Benadryl With Some of Its Derivatives and Certain Other Substances. Ellis, F. W.: J. Pharmacol. & Exper. Therap. **89**: 214, 1947.

Isolated guinea pig lungs were perfused through the bronchi at a constant rate. Histamine diminished the rate of perfusion and this effect was counteracted by a variety of compounds. Benadryl and B-monomethylaminoethyl benzhydryl ether induced an increase over the control outflow. These compounds also completely counteracted constriction induced by barium and by pilocarpine. K.

The Quantitative Estimation of Egg and Chicken Proteins in Equine Encephalomyelitis Vaccines. Engel, L. L., and Randall, R.: J. Immunol. **55**: 325, 1947.

Equine encephalomyelitis vaccines were analyzed for the presence of undesirable proteins of egg and chick embryo origin by the quantitative precipitin-reaction. Standardization curves were prepared by mixing varying quantities of egg and chicken-serum proteins with 1.0 ml. of homologous rabbit antisera. The total nitrogen content of the precipitate was calculated by subtracting the value of the serum blank control from the nitrogen value of the precipitate. The vaccines were similarly analyzed. Nonpurified horse and commercial human vaccines contained ovalbumin varying from 42 to 114 micrograms protein nitrogen per ml. and chicken-serum albumin varied from 60 to 80 micrograms protein nitrogen per ml. Ovoglobulin and chicken-serum globulin were present in smaller quantities. Purified vaccines contained considerably less egg and chicken proteins. E. WALZER.

Studies on the Antiallergic Effects of Vitamin P (Citrin) I and II. Hillstrung, H. A., and Hach, K.: Ztschr. f. Immunitaetsf. **100**: 6, 1941; **103**: 327, 1943.

The effects of citrin and other vitamin components on epidermal sensitization with dinitrochlorbenzol (DNB) in guinea pigs were studied. Nicobion (0.2 to 0.4 mg.) given prior to or following sensitization had no effect on the degree of sensitization induced. Although a slight loss in the sensitizing effect of DNB was noted when lactoflavin was administered prior to sensitization, its administration following sensitization produced only a negligible reduction in sensitization. When 150 mg. of citrin, with or without ascorbic acid, was administered prior

to sensitization, it had no effect on sensitization. When administered following sensitization, there was a marked reduction in the intensity of the contact reactions elicited by DNB. This effect of citrin was thought at the time to be a nonspecific one and was attributed to increased resistance of the cell membrane. Further studies with DNB revealed that the inflammation produced by a positive patch test reaction was of a serous type and if the area involved was large enough, blood changes (e.g., hematocrit, sedimentation rate) consistent with serous inflammations could be demonstrated in affected animals. The administration of citrin following sensitization prevented the hematocrit and other blood changes usually noted following severe patch test reactions. Seventy-five mg. or 150 mg. of citrin injected with or without lactoflavin had no effect on the production of anaphylactic shock in guinea pigs. H.

Miscellaneous

Increased Reactivity Caused by Adrenalin. Cameron, D. E.: Am. J. M. Sc. **213**: 331, 1947.

In a group of forty-two patients suffering from tensional anxiety states, adrenalin was found to produce three types of reactions: (1) headache, (2) increased cardiovascular activity, and (3) venous phenomenon. Headaches occurred in seven patients in the series. They were of sudden onset, usually occipital in location, and commonly appeared when the systolic pressure rose above 170 or when the difference between the preinjection and the postinjection pressures was more than 50. Deep massage of the occipital muscles and the back of the neck was the most effective measure for relieving these headaches. The cardiovascular response occurred in every patient in this group and consisted of increases in blood pressure and pulse rate which often continued over a period of several days. This is contrary to the usual experience that repeated administration of adrenalin over an extended period of time tends to reduce the reactivity of the pulse and blood pressure to the drug. It was usually necessary to reduce the dose of adrenalin by 50 per cent for seventy-two hours after this phenomenon occurred in order to avoid the accompanying headaches. It was also noted that, for several days following the administration of excessive doses of adrenalin, the cardiovascular system reacted with an increased pressor response to further adrenalin administration and with increased basal blood pressure and pulse levels. The venous phenomenon consisted of blanching and "goose pimples" along the course of small veins used for the intravenous injections of adrenalin. This reaction could be eliminated by the intravenous injection of histamine into the veins affected. F.

A Toxicologic Study of Two Histamine Antagonists of the Benzhydryl Alkamine Ether Group. Gruhzit, O. M., and Fiskin, R. A.: J. Pharmacol and Exper. Therap. **89**: 227, 1947.

Acute and chronic toxicity studies were carried out with benadryl and B-morpholinoethyl benzhydryl ether (A-446), a compound having about half the effectiveness of benadryl in counteracting the effects of atomized histamine in guinea pigs. The toxicity of A- 446 was about one-half that of benadryl. The toxic manifestations of the two compounds were identical. Acutely intoxicated dogs and rats evidenced apprehension, painful skin sensations (rats chewed off their feet), hypersensitivity to sound, convulsions, prostration, and respiratory and cardiac failure. Barbiturate sedation lessened the excitement but did not decrease the respiratory and cardiac depression or the mortality. Autopsies showed congestion of the visceral organs in animals dying of over-

dosage. Surviving animals did not show these changes. Chronic toxicity was investigated in mice and rats and a few dogs. The latter showed alertness, spastic extremities, slight incoordination, and painful skin sensation when doses of over 25 mg. per kilogram per day were administered. Divided doses were better tolerated than an equivalent single daily dose. In five dogs observed for almost six months, there was no cumulative effect. Mice and rats that died showed cachexia, congestive stasis with edema and superimposed inflammatory foci in the lungs, edema and mild fatty degeneration of the liver, colloid depletion of the thyroid, and congestion of the spleen. Benadryl in 1 per cent solution produced marked local irritation when injected intramuscularly or subcutaneously in mice, rats, and guinea pigs. Dogs tolerated the solution somewhat better. Attempts to induce anaphylactic sensitivity to benadryl in guinea pigs were unsuccessful. K.

Comparative Activity of Various Antihistaminic Substances Towards the Vasodepressor Response of Histamine. March, D. F., and Davis, A. J., Jr.: J. Pharmacol. and Exper. Therap. **89**: 234, 1947.

Ten antihistaminic drugs including benadryl, pyribenzamine, antergan, and a thienylglycolate (0-2,315) were quantitatively compared as to their antagonism of histamine-induced hypotension in anesthetized dogs, rats, guinea pigs and rabbits, and in pulmonary hypertension in the cat. The four drugs named above were found to be most effective. The range of effectiveness calculated as the number of molecules of antihistaminic compound per molecule of histamine antagonized varied widely with the reactive tissue and with the size of the protective dose. For example, one molecule of pyribenzamine counteracted the effect of one molecule of histamine on intact or isolated guinea pig lung and of five or six molecules of histamine on isolated guinea pig ileum. About ten molecules of the other antihistaminic compounds were needed to antagonize the effect of a single molecule of histamine on bronchi, uterus or gut. About a thousand molecules of pyribenzamine, benadryl or 0-2,315, the three most promising compounds, were needed, however, to counteract the effect of one molecule of histamine on the blood pressure of the dog. Larger amounts of the protective drugs antagonized proportionately greater amounts of histamine. No one of the drugs studied had an appreciable pharmacologic advantage over all the others. The clinical choice will probably be the drug with the least undesirable side effects. K.

Dispersal of Respiratory Pathogens in Relation to the Occurrence and Control of Air-Borne Infections. Robertson, O. H.: Am. Rev. Tuberc. **55**: 109, 1947.

Dust and droplet transmission of pathogenic bacteria can be controlled in hospitals. The major sources of the bacteria were floor dust, bedding, and nasal carriers. Oiling of the floors and blankets diminished the bacterial counts as much as 90 per cent. Blankets, rinsed in an emulsion of mineral oil, a synthetic detergent and water, were softer and warmer, but otherwise appeared and felt like untreated blankets. The treated blankets are not a fire hazard, and no skin irritation has been traced to them after extensive trial. K.

Allergy Abstracts

Asthma and Hay Fever

A Case of a Large Overdose of Epinephrine. Horwitz, O.: Am. Heart J. **33**: 107, 1947.

Through an error, 7 ml. of 1:1,000 solution of epinephrine was injected intramuscularly in the buttock of a 21-year-old male suffering from urticaria. The patient was immediately put to bed, an ice pack was applied to the injection site, and 0.4 Gm. of sodium amytal was administered orally. No unusual reactions were noted except for a slight headache which was relieved by aspirin and codeine. The maximum pulse rate was 128 per minute and the blood pressure rose to 220/96. Electrocardiographic findings were essentially normal except for tachycardia. The blood pressure and pulse rate returned to normal limits five hours later. K.

Effect on the Heart of an Overdose of Epinephrine. Report of a Case. McGinty, A. P., Baer, L. S.: Am. Heart J. **33**: 102, 1947.

Inadvertently, 5.0 ml. of a 1:1,000 aqueous solution of epinephrine was injected intramuscularly in a 29-year-old male believed to have malaria. The patient immediately experienced precordial distress and severe headache. The heart sounds became rapid and irregular, and the radial pulse became imperceptible. Five minutes later the blood pressure was 120/80. At ten minutes, the patient vomited. At thirty minutes, the pulse was 140 per minute and the blood pressure was 190/60. Twenty-three hours later, the patient was hospitalized complaining of constricting chest pain, dyspnea, and headache. His temperature at this time was 101° F., pulse 105 per minute, and blood pressure 94/60. Electrocardiographic changes suggestive of myocardial infarction persisted for over one month. Left temporal headache also continued for almost a month. Further convalescence was uneventful. K.

Continuous Intravenous Aminophyllin Therapy in Status Asthmaticus. Goodall, R. J., and Unger, L.: Ann. Allergy **5**: 196, 1947.

Aminophyllin in doses up to 3 Gm. per day dissolved in physiologic saline or in 5 per cent glucose in water was safely administered by continuous intravenous drip to ten patients in status asthmaticus. The dose of the drug was gradually reduced as relief of symptoms was obtained. Four patients experienced complete relief of symptoms, and some improvement was noted in five. Relapses occurred in some cases when therapy was discontinued.

E. WALZER.

"Ethyl-Nor-Epinephrine," A New Drug for Symptomatic Relief of Bronchial Asthma. Preliminary Report. Bubert, H. M., and Doenges, J. P.: Bull. School of Med. U. of Maryland **31**: 12, 1946.

Ethyl-Nor-Epinephrine (racemic 1-(3,4-dihydroxyphenyl)-2-amino-1-butanol hydrochloride) was administered intramuscularly in doses of from one to four milligrams to forty asthmatics. Of sixty-six attacks treated, relief was rated as 100 per cent in twenty-two attacks, 75 per cent in eighteen, and 50 per cent in twelve. Vital capacity during an attack was increased following the

administration of the drug. In twenty-one attacks of severe asthma in sixteen patients, the drug was administered intravenously in doses of one to ten milligrams (average 2.4 mg.). The systolic blood pressure fell an average of 16 mg. mercury, and the diastolic pressure dropped 8 mg. The hypotension began immediately and lasted for at least a half hour. Side reactions observed consisted of nervousness, fainting and generalized cutaneous erythema. Some patients stated that the drug was more efficacious than adrenalin. Most patients preferred the Ethyl-Nor-Epinephrine because of its "freedom from pressor effects and central nervous system stimulation." The drug has been used freely for eighteen months in the University of Maryland Allergy Clinic and by the patients at home without any serious reactions. K.

Aerosol Penicillin. Prigal, S. J., McGavack, T. H., Speer, F. D., and Harris, R.: J. A. M. A. **134**: 932, 1947.

Aerosol penicillin produced prolonged high blood penicillin values when propylene glycol combined with 5 per cent glycerine was used as the diluent. The various methods successfully employed for the inhalation of the medicated aerosols were: (1) the open method; (2) the air-tight chamber; (3) the tent; and (4) the closed breathing box. The latter method was the most effective in achieving high, long-lasting blood penicillin levels. The tent method was also highly effective and is best suited for the treatment of infants and children or cases where continuous treatment with penicillin is indicated. The prolonged high blood penicillin levels were partly due to the propylene glycol which was shown to have a definite antibiotic effect when mixed with serum. F.

The Antihistamine Action of N-(2-Pyridyl)-N-(2-Thenyl)-N′, N′-Dimethylethylenediamine Hydrochloride. Lee, H. M., Dinwiddie, W. G., and Chen, K. K.: J. Pharmacol. and Exper. Therap. **89**: 83, 1947.

N-(2-pyridyl)-N-(2-thenyl)-N′-N′-dimethylethylenediamine hydrochloride, known as "01013," is a compound similar to pyribenzamine. It relaxes histamine-contracted guinea pig intestine, counteracts the effect of atomized histamine on the guinea pig, reduces the depressor response of cats to histamine, and augments the pressor response of cats to epinephrine. Its acute toxicity for mice is comparable to that of pyribenzamine. Seven human subjects were given from 10 to 50 mg. of "01013." One subject reported a "light feeling" and one an "irritated stomach." Twenty-nine hay fever sufferers were given this drug in the fall of 1946 and in "a majority" of them, symptoms were alleviated.

Use of Intravenous Ethyl Alcohol in the Treatment of Status Asthmaticus. Brown, E. A.: Ann. Allergy **5**: 193, 1947.

Six patients in status asthmaticus were given 50 ml. of 95 per cent ethanol in 1,000 ml. of 5 per cent glucose in saline intravenously. Epinephrine 1:1,000 in doses up to 1 ml. was added to some of the infusions. About 100 ml. of the infusion was administered within the first ten minutes, and thereafter the flow was regulated at 70 to 100 drops per minute. Twenty-five infusions were given to six patients, of whom five experienced relief of their asthma. The typical reaction to the treatment was one of refreshing sleep lasting about three hours, a reduction in respiratory rate, and relief of asthma. No ill effects were observed. E. WALZER.

Dermatology

Tripelennamine "Pyribenzamine" Ointment for the Relief of Itching. Feinberg, S. M., and Bernstein, T. B.: J. A. M. A. **134**: 874, 1947.

Topical application of 2 per cent tripelennamine hydrochloride in either water-soluble or anhydrous base ointments was found to alleviate pruritus in the majority of patients suffering from itching dermatoses. The most satisfactory results were obtained in atopic dermatitis and pruritus ani. Improvement was also obtained in two cases of contact dermatitis of the eyelids and in several dermatitides of unknown origin. In one of five cases of urticaria, improvement followed local application of the ointment to the individual lesions. This ointment is not a substitute for such local medications as aluminum acetate solution, tar, or naphthalene ointments. F.

The Treatment of Dermatitis Venenata (Rhus) by Cryotherapy. Robinson, M. M.: J. Invest. Dermat. **8**: 239, 1947.

Liquid air, carbon dioxide snow, and ethyl chloride were compared in the treatment of 101 patients with poison ivy. Ethyl chloride was found to be the most efficient therapeutic agent of the three. Among 96 cases treated with an ethyl chloride spray, the average duration of the disease was five days. The average number of treatments was three administered at 24-hour intervals. Five cases were complicated by secondary infections and failed to respond to the therapy. E. WALZER.

A Study of the Action of Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in the Skin of Human Beings. Leavitt, M. D., Jr., and Code, C. F.: J. Lab. & Clin. Med. **32**: 334, 1947.

One microgram of histamine base, injected intracutaneously, was used to induce flares in thirty-three nonallergic persons. The flare was reduced 62 per cent when the histamine was superimposed on benadryl-infiltrated skin, 52 per cent when 150 mg. benadryl was administered intravenously, and 33 per cent when 150 mg. benadryl was given orally. Benadryl infiltrated in the skin caused local anesthesia. A procaine solution of anesthetic potency equivalent to that of a given benadryl solution reduced the histamine flare 23 per cent and only for as long as the anethesia remained. The benadryl solution, on the other hand, produced an 80 per cent reduction in the flare and the effect persisted beyond the period of anesthesia. K.

The Treatment of Gold Dermatitides. Use of Bal (2,3-Dimercaptopropanol). Ragan, C., and Boots, R. H.: J. A. M. A. **133**: 753, 1947.

BAL was used in the treatment of five patients with rheumatoid arthritis who developed dermatitis following the administration of gold compounds. All of these patients showed a definite increase in the excretion of gold through the urine coincident with the BAL treatment. The rash promptly subsided in the four patients who had their dermatitides for less than two months prior to the beginning of the BAL therapy. The fifth patient whose rash had been present for three months showed little improvement from the BAL. F.

Benadryl in the Treatment of Certain Diseases of the Skin. O'Leary, P. A., and Farber, E. M.: J. A. M. A. **134**: 1010, 1947.

Benadryl was highly effective in the treatment of angioneurotic edema and acute and chronic urticaria. Withdrawal of the drug was usually followed

by recurrence of the lesions. Only eight of twenty-five patients with atopic dermatitis experienced relief from the pruritis, and only six of thirty-eight patients with other types of pruritic diseases were relieved. The edematous stage of scleroderma and acrosclerosis was favorably influenced by the drug. Side reactions occurred in fifty-eight of the one hundred eighty-six patients in this series, but in only ten patients were these reactions severe enough to warrant discontinuance of benadryl. F.

Clinical Use of a New Antihistaminic Compound (Pyribenzamine) in Certain Cutaneous Disorders. Osborne, E. D., Jordon, J. W., and Rausch, N. G.: Arch. Dermat. & Syph. **55**: 309, 1947.

Pyribenzamine was administered to eighty-nine patients with various cutaneous disorders. Twenty-three of twenty-four patients with acute urticaria obtained prompt relief after taking the drug in doses of 100 to 400 mg. per day for two to fourteen days. Nine of fifteen patients with chronic urticaria were definitely benefited, and six obtained no relief. In six of the nine benefited patients, urticaria recurred within twenty-four hours after use of the drug was discontinued. However, relief was again obtained when the drug was readministered. In nineteen of thirty patients with chronic atopic dermatitis, the pruritus was relieved by about 50 per cent during the daily administration of 100 to 400 mg. of pyribenzamine for two to sixteen weeks. Three of the nineteen cases experienced relief of pruritus within twenty-four hours and the remaining patients were decidedly improved after two weeks. Itching recurred when the medication was stopped and was again relieved by readministration. Pyribenzamine failed to influence the symptoms or lesions in fifteen patients with dermatitis venenata. Excellent results were obtained in two cases of physical allergy, one sensitive to sunlight, the other to cold. Three of four patients with dermatitis herpetiformis obtained relief. The administration of pyribenzamine prior to skin testing decreased the size of the wheals in eight of fifteen cases. The effectiveness of pyribenzamine in reducing the size of the wheals could not be correlated with its subsequent therapeutic effect in the same patient. C.

Role of Food Allergy in Eczematoid Dermatitis. Flood, J. M., and Perry, D. J.: Arch. Dermat. & Syph. **55**: 493, 1947.

Trial diets, elimination diets, and food diaries were resorted to in thirteen cases of persistent "eczematoid dermatitis" in which routine scratch and intracutaneous tests failed to reveal specific sensitivities. Food sensitivity was found to be the primary etiologic factor in these cases. Trial diets appeared to be the most satisfactory method for discovering the offending foods. Superimposed pyogenic and trichophytic infections must be recognized and eliminated before testing can be interpreted. Detailed case reports illustrating each of the diagnostic methods used are presented. C.

Otorhinology and Ophthalmology

Experimental and Clinical Observations Regarding the Nasal Vasoconstrictor Action of Oenethyl and EA-83. Shirkey, H. C., and Jackson, D. E.: Ann. Otol. Rhin. & Laryng. **55**: 859, 1946.

The experimental effects of Oenethyl (EA-1) and EA-83 (2-methylamino-6-hydroxy-6-methyl heptane) on the nasal mucous membranes of animals and man are presented. In the animal experiments, the nasopharynx of anesthetized dogs was closed off by means of a soft rubber ball, and tightly fitting nasal tubes were hooked up to a sensitive tambour and a smoked drum. Thus a graphic record was obtained of the effects of intranasal and intravenous administration of the

drugs. In man, a modification of the Sternstein-Schur apparatus was used. Both Oenethyl and EA-83 are active vasoconstrictors of the vessels in the nasal mucosa. Both drugs are active in man over a period of five hours, oenethyl being the more active of the two. Although the use of the drug locally or intravenously was accompanied by a rise in blood pressure in animals, its use in the nose in human beings had no bad side effects. C.

Sinusitis and Allergic Diseases. Grove, R. C.: Am. Pract. **1**: 468, 1947.

Infections of the sinuses are an important factor in a large number of allergic disturbances. In the primary stage of the hyperplastic type of sinusitis, allergic manifestations are present in almost 100 per cent of cases. In bacteriologic studies made on hyperplastic membranes, positive cultures were obtained in 80 per cent of cases. Antral membranes gave a higher percentage of positive cultures than did either ethmoid or sphenoid membranes. Positive cultures were frequently obtained from the sinal membrane in patients who showed negative antral washing cultures. The diagnosis of hyperplastic sinusitis requires careful clinical, physical, x-ray, and laboratory examinations. Nasal examinations must include anterior rhinoscopy and the use of the nasopharyngoscope. Transillumination must be supplemented by x-ray. Lipiodal or umbrathor often helps in outlining polyps. Cytologic examination of the nasal and sinus secretions often reveals the presence of eosinophiles. Elimination of other foci of infection must also be effected. Hay fever is often complicated by sinusitis, and specific therapy may be materially helped by a washing. Treatment of the sinusitis must be conservative during the pollen season. Sinusitis may be a primary or a secondary cause of vasomotor rhinitis, urticaria, and asthma. Sinus surgery must be adequate and, in order to effect good results, the entire diseased membrane must be removed. Of two hundred asthmatic patients who were subjected to sinus surgery 69 per cent experienced marked relief from their symptoms. Of those from whom all the diseased sinus tissue was removed, 79.8 per cent showed improvement, while partial removal produced improvement in only 35.2 per cent. In asthmatic patients with specific sensitivities and associated sinusitis, there was a 16.4 per cent greater improvement than was obtained in the pure infective cases.

Best results from the operative procedures were obtained in those patients whose asthma began after the age of twenty-one and in whom the duration of asthma was less than ten years and the age at operation was between 31 and 50 years. The shorter the duration of the asthma, the better the results. The usual types of injection therapy, such as house dust and vaccine (stock and autogenous) were used postoperatively in most cases. F.

Maxillary Sinus Drainage. Van Alyea, O. E.: Ann. Otol. Rhin. & Laryng. **55**: 754, 1946.

The maxillary ostium in a healthy state provides an adequate drainage outlet for the maxillary sinus. In acute sinusitis, swelling of the mucosa constricts the lumen of the ostium, thus retarding or blocking completely the discharge of pus from the cavity. Recovery takes place when the edema has subsided sufficiently to permit an outflow of secretions as rapidly as they accumulate. Among the factors which cause drainage impairment and prolongation of infection are anatomic defects, obstructing polypi, and the generalized mucosal edema of an uncontrolled allergic condition. The swelling noted on roentgen examination is the normal tissue reaction to disease, and the swelling remains as long as the membranes are subjected to irritants, whether they be pathogens, allergens, or merely the toxic irritation of a stagnant exudate. In a study of sections of tissues removed by radical procedures from 82 patients,

no membrane was found which was so diseased as to be considered beyond hope of repair. In the majority of cases, eosinophiles were found, indicating that allergy is a dominant factor in the maintenance of chronic sinus disease. A plea is made for conservatism in the management of chronic maxillary sinusitis. C.

Irradiation of the Nasopharynx. Crowe, S. J.: Ann. Otol. Rhin. & Laryng. **55**: 779, 1946.

Lymphoid tissue is an integral part of the mucous membrane of the posterior and lateral walls of the pharynx and nasopharynx. It may hypertrophy as a result of infection or allergy. Nodules of hyperplastic and infected lymphoid tissue in the nose, near the posterior end of the middle turbinate, may cause symptoms resembling vasomotor rhinitis. Infection plays an important role in the development of respiratory allergy, the primary focus being the lymphoid tissue in the pharynx and nasopharynx. In children, asthmatic symptoms which improve following tonsillectomy and recur at a later date are often traced to the regrowth of adenoid tissue. Irradiation with the nasopharyngeal radon or radium applicator is the treatment of choice for the removal of lymphoid tissue in locations inaccessible to ordinary surgical measures. The technique of irradiation is presented in detail. C.

Miscellaneous Allergies

Changes in the Electrocardiogram During Allergic Shock. Castberg, T., and Schwartz, M.: Acta. Med. Scandinav. **126**: 459, 1947.

After reviewing the literature on changes in heart function during acute anaphylactic shock in animals, the authors concluded that such changes could be attributed to anoxia of the myocardium, and were probably not the result of antigen-antibody reactions in the myocardium. So far there has been no convincing evidence that allergy plays a role in the production of paroxysmal tachycardia, hypertension, or coronary thrombosis. A more convincing causal relationship has been demonstrated in the various cardiac phenomena which may occur following serum sickness.

Electrocardiographic studies were made on five hay fever patients during typical constitutional reactions following tests or dosage. Adrenalin was withheld until the electrocardiogram tracings were recorded. The distinct electrocardiogram changes, noted in all five cases, were of a similar pattern. The frequency of the heart beat increased, P2 increased and R1 and R2 decreased. The T waves were flattened in Leads I and II. In one case a positive T3 became negative. In three cases the S-T segment was depressed in Lead II. The P-Q, QRS and Q-T intervals showed little change. The electrocardiogram changes described are typical of those encountered during experimental oxygen deficiency tests.

No electrocardiogram changes were observed which could not be attributed to myocardial anoxia. Since all five patients were dyspneic, it may be assumed that there was insufficient oxygen saturation of the blood in the lungs, although local circulatory disturbances in the heart could not be excluded. There was no evidence that a specific antigen-antibody reaction took place in the heart of human beings during the "allergic shock." A very low pulse during shock may be due to a vagus effect and may cause death unless 2 mg. of atropine are given intravenously. H.

Streptomycin Toxicity. Reactions to Highly Purified Drug on Long-Continued Administration to Human Subjects. Farrington, R. F., Hull-Smith, H., Bunn, P. A., and McDermott, W.: J. A. M. A. **134**: 679, 1947.

Although impure streptomycin is usually well tolerated, there have been four general types of reactions observed following its use. These reactions have been classified as follows: (1) the so-called histamine reaction, characterized by flushing, headache, and abrupt fall in blood pressure; (2) anaphylactic reactions; (3) neurologic reactions, characterized by vestibular dysfunction and occasionally by deafness; and (4) the renal reaction characterized by cylindruria accompanied by impaired renal function. The effects of long-term administration were studied on a group of sixteen adult subjects suffering from active pulmonary tuberculosis. A highly purified lot of streptomycin was administered daily over a period from one hundred to one hundred twenty days. The drug was well tolerated and caused less local irritation than did the impure form. However, all the manifestations of toxicity observed with the impure streptomycin, with the exception of the histamine reaction, were noted with the highly purified streptomycin sulfate. The purified form still contained about 5 per cent impurities, and these may have been responsible for the reactions. It was necessary to interrupt therapy in only two cases. In both instances, the reactions appeared in the ninth day of treatment, were of the anaphylactic type, and consisted of a maculopapular pruritic eruption over the trunk and extremities, pyrexia, nausea, vomiting, hypotension, and eosinophilia. The symptoms subsided after one week and, following a rest period of several weeks, it was possible to resume administration without untoward effects. An intermittent or sustained eosinophilia ranging from 5 to 39 per cent was noted in fourteen of the sixteen patients. The eosinophilia always diminished gradually to below 5 per cent in from four to six weeks after cessation of therapy. Cylindruria occurred in the majority of the subjects usually in the presence of highly acid urine. In only two patients was renal function impaired and, in one of these, normal function returned despite continued therapy. Symptoms of vestibular dysfunction appeared uniformly between the seventeenth and the twenty-first day of treatment, but these symptoms disappeared with the continued use of the streptomycin. Deafness developed in two of the sixteen patients, occurring in both instances after repeated intrathecal administrations of streptomycin for the treatment of an ultimately fatal tuberculous meningitis. The fact that the highly purified streptomycin given over a protracted period produced only a small number of reactions justifies its use in the treatment of serious protracted illnesses. F.

Toxicity of Streptomycin. McDermott, W.: Am. J. Med. **11**: 491, 1947.

The use of purified streptomycin has eliminated the so-called histamine reaction and has reduced the incidence of reactions following topical applications. Allergic reactions to streptomycin consist of fever, dermatitis (with or without fever), and eosinophilia (with or without dermatitis). Serious results have not been encountered even when streptomycin therapy has been continued in the presence of allergic reactions. However, continued administration of the drug in the presence of reactions should be attempted only when the illness is so severe as to constitute a threat to life. When reactions occur during the course of treatment of tuberculosis, therapy should be discontinued and single test doses should be given at weekly intervals. Regular therapy can usually be resumed in three to four weeks when the test doses no longer evoke reactions. Neurologic and renal reactions occur with the purified drug; the former constitute the most important of the toxic reactions to streptomycin. It has been

demonstrated that the intramuscular administration of streptomycin in daily doses ranging between one and three grams is well tolerated for a one- to two-week period by most individuals and, except for the production of vestibular dysfunction, may be well tolerated for periods of as long as four months. F.

Tropical Eosinophilia in East Africa. Wilson, H. T. H.: Brit. M. J. **1**: 801, 1947.

Tropical eosinophilia or eosinophilic bronchitis was first described in 1940 in Southern India. The clinical picture is one of cough, fever, loss of weight, and high blood eosinophilia. The illness runs a prolonged but benign course. The x-ray findings in all cases consist of a mottling of both lung fields similar to that observed in miliary tuberculosis and silicosis. In six of thirty-four consecutive patients admitted to the hospital with a diagnosis of recurrent bronchitis or asthma, an eosinophilia of 40 to 78 per cent was found. These six patients complained of cough, wheezing, and low-grade fever. In the "symptom-free" intervals, only an early morning spasmodic cough was present. Three of these cases showed the typical mottling ("eosinophilic lung pattern"). Tubercle bacilli could not be detected in the sputum. Stool studies for parasites were negative except for the presence of ankylostoma in two cases. In all six cases the duration of illness was less than three years. Without the unusually high blood eosinophilia, a differential diagnosis from bronchial asthma or chronic bronchitis could not be made in these cases.

Several possibilities from the point of view of etiology are discussed. (1) *Allergy.*—A family and personal history of allergy is usually absent and the presence of fever, leucocytosis, splenomegaly, and the typical chest x-ray findings do not fit this diagnosis. (2) *Loeffler's Syndrome.*—In this condition the lung infiltrations are more often unilateral and usually transient. (3) *Specific Infection.*—The frequent finding of mites in the sputum, especially those of Acarus, has suggested the possibility of a lung infestation. (4) The successful treatment of these cases with arsenic may be significant. At present the author considers the etiology of this entity unknown. H.

Employment of Serological and Skin Tests in Outbreaks of Trichinosis in the Alingsas and Boras Districts (Sweden). Roth, H.: Acta. Med. Scandinav. **126**: 17, 1946.

The value of different specific methods of diagnosis in trichinosis is discussed. Because it is not always possible to demonstrate the parasites in stools, blood, or muscles of the patient, the writer prefers cutaneous and serologic tests. Intracutaneous and precipitin tests with antigen prepared from dried, pulverized, and extracted trichinella larvae yielded satisfactory diagnostic results. However, false positive and negative reactions occasionally occurred. The new microscopic precipitin test of Suessenguth and Kline with living larvae was found to be the most sensitive and specific diagnostic test. The test became positive during the second and third week after infection, and was still positive in four of five sera at the end of twelve months. H.

Intradermal Reaction in Trichomonas Infection. Adler, S., and Sadowsky, A.: Lancet **1**: 867, 1947.

The question as to whether vaginal infection with trichomonas produces any detectable immunologic reaction in the host was investigated. The preparation of Trichomonas vaginalis antigen is described in detail. Intracutaneous tests were performed on the forearm with 0.1 c.c. of the antigen. A positive reaction consisted of an area of redness, measuring from 1 to 2 cm. in

diameter, which appeared within several hours and faded after forty-eight hours. After a study of 102 patients, the authors concluded that direct microscopic examination gave better diagnostic results than did the cutaneous test. Only one case was detected by the cutaneous test before the diagnosis could be made by microscopic study. Trichomonas antigen is evidently absorbed through the vaginal wall and produces specific sensitization in the host. H.

Dermatitis Due to Quinacrine Hydrochloride ("Atabrine"). Nisbet, T. W.: J. A. M. A. **134**: 447, 1947.

The vast majority of dermatitides observed among men serving in the southwest Pacific were caused by atabrine. These eruptions were erroneously diagnosed as contact dermatitis, impetigo, pyoderma, erysipeloid eruptions, mycotic dermatitis, and seborrhea. Cutaneous reactions to atabrine may be classified as follows: (1) eczematoid (comprising about 80 per cent of the total number of cases); (2) hypertrophic lichenoid, 12 per cent; and (3) generalized exfoliative. Contact dermatitis, rhinitis, bronchitis and asthma may also follow the use of atabrine. Hepatic damage, hypoplastic anemia, visual disturbances, and psychoses may result from its ingestion. Immediate reactions to atabrine, such as pruritus, urticaria and exfoliative dermatitis are considered to be allergic in nature, while reactions occurring after prolonged administration are toxic in character. The drug should be discontinued at the first sign of toxic or allergic symptoms. The eczematoid lesions respond to local therapy. Secondary infections may be treated with penicillin. The lichenoid type of reaction requires little treatment other than a high caloric, high vitamin diet. F.

Anaphylaxis

A Quantitative Study of the Arthus Phenomenon Induced Passively in the Rabbit. Fischel, E. E., and Kabat, E. A.: J. Immunol. **55**: 337, 1947.

The skin responsiveness to egg albumin of rabbits passively sensitized at four to six cutaneous sites with antiegg albumin sera was compared with that of rabbits similarly sensitized at a single site. All sites tested with egg albumin one-half hour after sensitization showed reactions of equal size and intensity. When the sensitizing serum was administered intravenously and the skin was tested with albumin at three areas, the reactions were smaller than those obtained in rabbits tested with a single intracutaneous injection of antigen. No difference in reactions was noted at a single or at multiple sites when the antigen was first administered intravenously and the sensitizing serum was subsequently introduced intracutaneously (reversed Arthus phenomenon). Quantitatively, the intensity of reaction was primarily dependent upon the amount of antibody-nitrogen available at the site of contact with the antigen. The amount of antigen was not a factor once a threshold quantity had been exceeded. The intracutaneous injection of as little as 0.025 mg. antibody-nitrogen regularly produced minimal reactions regardless of the route of administration of the antigen. When the antibody was given intravenously twenty to forty times as much antibody was required to yield reactions of comparable intensity. "When reduced to an equal weight basis only three to seven times as much antibody gave a minimal Arthus reaction as gave fatal anaphylaxis" in the guinea pig.

E. WALZER.

The Effect of Thorotrast on Anaphylactic Shock in the Dog. Goth, A., and Holman, J.: J. Pharmacol. & Exper. Therap. **89**: 379, 1947.

Dogs sensitized with horse serum received from two to six milliliters of thorotrast from four hours to ten minutes prior to the injection of horse serum. Thorotrast in doses of four milliliters or more per kilogram prevented the hypo-

tension and increased the clotting time which occurred in control animals and in those receiving only two milliliters per kilogram of Thorotrast. Histamine shock was not prevented by Thorotrast. The injection of Thorotrast alone without the eliciting dose of horse serum *prolonged* clotting time. Thorotrast in vitro failed to coagulate dog blood in the presence of heparin. Thus the prevention of increased clotting time in Thorotrast-treated dogs subjected to anaphylactic shock could not be attributed to a direct effect of Thorotrast on the clotting mechanism. It is suggested that Thorotrast is more effective than India ink or iron oxide in blocking the reticulo-endothelial system and prevents the liberation of histamine and heparin in the sensitized dog. K.

A Study of Sensitivity to Hemophilus Pertussis in Laboratory Animals. 1: Hypersensitivity in Laboratory Animals to Hemophilus Pertussis. Parfentjev, I. A., Goodline, M. A., and Virion, M. E.: J. Bacteriol. **53**: 597, 1947.

Hemophilus pertussis filtrate was precipitated with ammonium sulfate, dialyzed and lyophilized. Mice were injected intra-abdominally with a 5 per cent solution of this material. Sensitization resulted as evidenced by death following the administration of a shock dose of the same material seven to ten days after the sensitizing dose. Control animals injected with a suspension prepared from the broth showed no reactions. Sensitization was also produced in guinea pigs by two intramuscular or one intra-abdominal injection of the concentrated filtrate. Studies were made in mice with boiled, nonboiled and formol-treated unconcentrated filtrate of hemophilus pertussis culture. It was found that the allergenic fraction of the hemophilus pertussis filtrate is heat stable while the toxic principle is heat labile. F.

A Study of Sensitivity to Hemophilus Pertussis in Laboratory Animals. II. Hemophilus Pertussis Allergen and Its Assay on Laboratory Animals. Parfentjev, I. A., Goodline, M. A., and Virion, M. E.: J. Bacteriol. **53**: 603, 1947.

Several fractions of hemophilus pertussis were prepared. One of the fractions gave positive biuret, xanthoprotein, Millon, Hopkins-Cole and Sakaguchi tests. Tests for nucleoproteins were strongly positive. This nucleic acid protein complex, referred to as NPD (nucleo-protein denatured), was found to be very stable as compared with other toxic substances previously isolated from nucleoprotein. The sensitizing property of NPD was much less than that of nucleoprotein organisms. Mice sensitized by an injection of hemophilus pertussis vaccine succumbed to NPD doses less than one-twentieth of those required to kill nonsensitive mice. Sensitized mice were also tested with NPD prepared from B. abortus, the allergenic fraction (AF) prepared from B. bronchiseptica culture, commercial tuberculin and various sera and broths. These mice could be shocked with the proteins of B. abortus and B. bronchiseptica, but not with the other materials. Further experiments demonstrated that it was the protein portion of the nucleoprotein and not the nucleic acid which was the shocking factor. NPD given in lethal and sublethal doses to guinea pigs caused various degrees of respiratory acceleration often leading to death, depending upon the size of the dose. Sensitized animals died in anaphylactic shock within nine minutes, while normal guinea pigs died of toxemia after from there to sixteen hours. The dosage required to produce death was much less in desensitized than in normal guinea pigs. In Dale bath studies, the uterine strips of highly sensitized guinea pigs contracted on the addition of a 1:100,000,000 dilution of NPD whereas normal uteri failed to respond to a 1:1,000,000 dilution. F.

A Study of Sensitivity to Hemophilus Pertussis in Laboratory Animals. III. The Formation of Antibodies and the Development of Sensitivity in Laboratory Animals Injected With Hemophilus Pertussis Antigens. Parfentjev, I. A., Goodline, M. A., and Virion, M. E.: J. Bacteriol. **53**: 613, 1947.

Anti-NPD (nucleoprotein denatured) rabbit serum was prepared and found to contain a high titer of antibodies against both nucleoprotein and the soluble antigens in culture filtrates of hemophilus pertussis. Antibacterial rabbit serum contained only traces of antibodies against nucleoprotein but did possess a high titer of antibodies against the soluble antigens in culture filtrates. Antibacterial serum agglutinated hemophilus pertussis organisms in high dilutions while anti-NPD serum possessed virtually none of these agglutinins. Guinea pigs passively sensitized with anti-NPD serum were highly sensitive to intracardial injections of NPD. Attempts at passive transfer of sensitivity with hemophilus pertussis antitoxic serum were not successful but some evidence of passive transfer of sensitivity to antibacterial serum was noted. An intraabdominal injection of anti-NPD serum was found to increase the sensitivity of guinea pigs to hemophilus pertussis vaccine. Sublethal doses of NPD desensitized passively sensitized guinea pigs, whereas hemophilus pertussis broth failed to desensitize. Passive transfer of sensitivity to NPD and desensitization with sublethal doses was also accomplished in mice. Local passive transfer of sensitivity to rabbit anti-NPD serum was also demonstrated. F.

Miscellaneous

Intratracheal Penicillin Therapy in Suppurative Bronchiectasis. Siltzbach, L. E.: Arch. Int. Med. **79**: 570, 1947.

Penicillin was administered intratracheally to thirteen patients with suppurative bronchiectasis. The patients ranged in age from 17 to 63 years and the symptoms of bronchiectasis had been present for from 2.5 to 28 years. Penicillin in doses of 100,000 units dissolved in 20 ml. of saline was introduced into the trachea and directed to the desired lobe by positioning the patient. Seven to fifteen instillations were given over a period of eleven to eighteen days. Intratracheal instillations were begun only when treatment with oral sulfonamides and penicillin intramuscularly or by nebulizer failed to produce further improvement. Immediate improvement was noted in ten patients who showed at least a 50 per cent diminution in their sputum volume. Four of the patients had a recurrence of symptoms within two months; the improvement in the other six continued from six to twenty-one months. The best immediate results were noted in two patients in whom intratracheal administrations of penicillin were combined with intramuscular injections. One patient, a child with atelectasis and suppurative pneumonia, showed immediate improvement and re-expansion of the lung following intratracheal therapy. Combined intramuscular and intratracheal penicillin therapy is suggested as a valuable adjunct in the preparation of bronchiectatic patients for lobectomy. E. WALZER.

Reticulo-Endothelial Immune Serum (REIS). VI. Production of Potent Serum by Anamnestic Reaction. Anigsten, L., Whitney, C. M., and Powerat, M. F.: Proc. Soc. Exper. Biol. & Med. **64**: 279, 1947.

Potent antiorgan sera were produced in rabbits by the administration of tissue suspensions from other animal species. Constant amounts of spleen and bone marrow from the guinea pig, rat, or chick suspended in saline were injected intravenously and similar amounts were given orally, at four-day inter-

vals for twelve days. When the immunized rabbits received a single intravenous injection of the same antigen about a month later, an anamnestic response occurred. The marked increase in antibody formation was demonstrated by complement fixation and by the tissue culture assay method. The latter method measures the potency of an antiorgan serum by its capacity to inhibit the growth of a tissue culture of the specific organ. J. SHERMAN.

Pharmacological Properties of Antihistamine Drugs Benadryl, Pyribenzamine, and Neoantergan. Sherrod, T. R., Loew, E. R., and Schloemer, H. F.: J. Pharmacol. and Exper. Therap. **89**: 247, 1947.

Benadryl, pyribenzamine, and neoantergan administered intravenously to anesthetized dogs were equally effective in counteracting the depressor response to a subsequently administered dose of from five to ten micrograms per kilogram of histamine. Only benadryl diminished the depressor response to acetylcholine. Pyribenzamine and neoantergan administered to guinea pigs prior to exposure to atomized histamine afforded greater protection than benadryl. The mean pressor response to epinephrine was enhanced 42 per cent by benadryl, 45 per cent by pyribenzamine, and 28 per cent by neoantergan; the duration of the pressor effect was prolonged by from 50 to 75 per cent. The prolongation of this pressor response was not affected by atropinization nor by vagotomy, indicating that the mechanism does not involve the cholinergic nerves. Spontaneous activity of the dog's uterus was not affected by benadryl, but pyribenzamine and neoantergan administered intravenously induced uterine contraction. Benadryl reduced the tone of the canine duodenum and inhibited its spontaneous activity for from ten to thirty minutes after intravenous injection. Neoantergan and pyribenzamine induced or increased duodenal tone within two minutes of their injection. All three drugs counteracted histamine-induced spasm of the duodenum. The acute toxicity of all three drugs on an equal weight basis was very similar. K.

Rutin in Purpura. Madison, F. W., and Pohle, M. D.: J. Lab. & Clin. Med. **32**: 340, 1947.

Citrin is the source of vitamin P which reverses experimentally induced vascular fragility. Rutin, a flavonol glucoside closely related to one of the break down products of citrin, has been used in 173 cases of purpura and is credited with reversal of the fragility in 88 per cent of these patients. Rutin was administered by the author to fourteen cases of purpura. Of these patients, four had advanced malignancies, and one had hypertension and retinal hemorrhages. In six the purpura was probably allergic in origin, in one it was toxic and in one it was endocrine. The best results were obtained in the patients with malignancy. Less striking results were observed in the allergic group. The response in other cases was questionable. K.

Allergy Abstracts

Asthma and Hay Fever

Allergy Due to Fungi. Nilsby, Ivar: Svenska Läkartidningen n:r 17, 1947.

The author has made a mold spore survey, the first in Sweden, using the Petri plate method. Exposures were made thirty minutes daily on the fourth floor of his home from August to December, 1946. The greatest concentration occurred in the last days of August, decreasing during the defoliation period, and increasing in misty weather. The concentration was low during the winter, but even in severe cold spores were found. Hormodendrum was the most common fungus found outdoors in Sweden. Penicillium, Pullalaria, and yeast-like fungi, in that order, were the next most common outdoor fungi. Penicillium was most common indoors, and did not show seasonal fluctuation. In indoor studies, plates were exposed for fifteen minutes in different apartments. The number of colonies ranged from none to more than one hundred on one plate. In one home, twenty-five Alternaria colonies were found. This fungus is very uncommon in Sweden. In some other homes, an almost pure culture of *Monilia tropicalis* was obtained. Plates have been exposed one Swedish mile outside of Örebro during the same period exposures were made in the city. Exposures were also made in Stockholm and Gothenburg (large cities) and in Lund (small city). The greatest mold concentration occurred in the country and in small cities.

On plates exposed in an aeroplane, large numbers of spores were found up to two hundred meters, and occasionally up to seven hundred meters. None were found at altitudes over one thousand meters. Mist increased the number of spores. Rain had no influence. The spores seemed to follow the ascending air currents. When the moisture condensed to mist, the spores adhered to the small drops of water. Very high spore counts were found in barns and thresh-ing mills. Fifteen per cent of 276 allergic patients gave positive skin reactions to mold extracts. The most common complaints in this group were asthma and chronic rhinitis.

BENGT NORÉN.

Penicillin Inhalation Therapy. Segal, M. S., Levinson, L., and Miller, D.: J. A. M. A. **134**: 762, 1947.

A total of 118 patients with various types of respiratory diseases, including bronchial asthma, purulent sinusitis, bacterial pneumonia, infective laryngo-tracheobronchial edema, bronchiectasis, and pulmonary abscess were treated with aerosol penicillin, given in six to eight daily doses of 25,000 units each. Purely local pulmonary infections without bacteremia could be favorably in-fluenced without attaining high blood penicillin levels. Supplemental intra-muscular doses of penicillin were administered to patients with toxemia or septicemia. Aerosolization was usually effected by means of oxygen flowing through a two liter vaponephrin nebulizer which permits the utilization of ex-pired penicillin. For patients with obstructive diseases of the respiratory tract a helium-oxygen mixture was used in place of oxygen, and, in cases with tracheo-bronchial obstruction, the penicillin was introduced through tracheotomy

openings. Good results were obtained in bacterial pneumonia, pulmonary emphysema, acute laryngotracheobronchial edema, and in the aerobic non-odoriferous postpneumonic type of pulmonary abscess. Fair results were noted in bronchiectasis, while only a very small percentage of cases of bronchial asthma showed improvement. Treatment occasionally caused edema of the lips or mucosa of the mouth and generalized urticaria. These reactions were most common among the asthmatic patients. Two patients under treatment for chronic bronchitis and emphysema developed their first attacks of bronchial asthma while receiving treatment with the aerosol penicillin, and cleared after cessation of the therapy. Indiscriminate use of penicillin aerosol is discouraged, and identification of the etiologic organisms to establish their penicillin sensitivity is essential before using this type of therapy. F.

Allergic Reactions From Handling Penicillin. MacInnes, K. B.: Ann. Allergy **5**: 102, 1947.

A nurse, who had received penicillin and sulfonamides therapeutically, developed generalized pruritus and urticaria of the legs within forty-eight hours after handling both drugs. Subsequently, she developed nasal congestion after entering a room where penicillin was being prepared. Patch and scratch tests were performed with both drugs. Positive reactions were obtained to penicillin only. Intracutaneous tests with penicillin spores were negative. In another nurse, erythema, pruritus, urticaria, and a papular rash of the face and arms, as well as photophobia and nasal congestion, appeared after repeated handling of penicillin. On subsequent re-exposures, these symptoms recurred and were associated with conjunctivitis and edema of the eyelids. Six hours after a drop of penicillin was applied to the arm, this patient developed itching and erythema at the site. Hence, "urticaria, photophobia, and nasal congestion are reported for the first time as a result of contact with the drug."
E. WALZER.

Inhalation Therapy in Chronic Bronchial Infection. Levine, E. R.: Dis. Chest **13**: 295, 1947.

Inhalation therapy with penicillin was administered to a group of forty-two patients with bronchiectasis of many years' duration. All of the patients had bronchographic evidence of bronchiectasis and had been treated unsuccessfully with bed rest, postural drainage, oral sulfonamides, and parenteral penicillin. The ages of the patients ranged from 8 to 80 years, and the duration of symptoms varied from eight to sixty-four years. Among the more common organisms found in the sputa were hemolytic and nonhemolytic streptococci, streptococcus viridans, staphylococcus aureus, bacillus proteus, and Friedlander bacillus. Penicillin aerosol was administered every three hours over a period of three to four weeks in doses of 1,000 to 20,000 units in one milliliter solution. Of the forty-two cases, nineteen experienced complete cessation of symptoms, fourteen had some relief, and eight showed no improvement. Only nine of thirty-three maintained their improvement. Recurrences were generally marked by a change in bacterial flora indicating new infections. Blood levels of penicillin observed in these patients were not of therapeutic significance, although normal patients inhaling similar concentrations had high levels. Good results were obtained in patients harboring organisms sensitive to penicillin. It was concluded that inhalation therapy is of definite value in the treatment of bronchial infection. Limitations of this type of therapy are dependent upon the chemotherapeutic agent employed and not on the technique.
E. WALZER.

The Symptomatic Treatment of Hay Fever With Diaminobenzopyridyl HCl (N′-Pyridyl-N′-Benzyl-N-Dimethylethylenediamine Hydrochloride) (Pyribenzamine). Leibowitz, H., Kutrz, I. M., and Schwartz, E.: New York State J. Med. **47**: 989, 1947.

Pyribenzamine in doses of 50 mg. was administered twice daily to eighty-five patients with ragweed hay fever. Symptomatic relief was obtained in nine of twenty-one patients with pyribenzamine alone, in thirty-five of forty-seven patients who received pyribenzamine and ragweed desensitization, and in ten of eighteen patients who received only specific treatment. Twenty-five of sixty-eight patients experienced side reactions, such as sleepiness, drowsiness, palpitation, nervousness, weakness, headache, nausea tinnitus, dizziness, and dryness of the mouth. The authors stress the fact that this study was done in 1946, when the pollen count in New York City was exceptionally low. C.

Timothy Versus Bermuda Grass. Wodehouse, R. P.: Ann. Allergy **5**: 137, 1947.

Two sera, each containing reagins for timothy and Bermuda grass, were studied. Sizable passive transfer reactions were obtained with JB serum (Class A) in dilutions of 1:1,200 when sites were tested with timothy (100 N. units) or Bermuda grass (1,500 units). The BR serum (Class B-C) transfered in a dilution of 1:80 for Bermuda grass and at 1:20 for timothy. When sites of JB serum in various dilutions were tested with the antigens in equal nitrogen concentration, the timothy reactions were always larger than those with Bermuda. In BR serum sites, the reverse was true. In other experiments, the sera were mixed with serial dilutions of antigen in vitro. The sites which were sensitized with the mixtures were first tested with homologous antigen, and then retested with heterologous antigen. Timothy almost completely neutralized its sites against Bermuda, but Bermuda did not neutralize its sites to timothy. With the BR serum, timothy did not neutralize its sites to Bermuda, but Bermuda sites were neutralized to timothy. In in vivo cross neutralization experiments, timothy completely desensitized JB serum sites to both antigens but not BR sites to Bermuda. Bermuda completely desensitized BR serum sites to both antigens but not JB serum sites to timothy. It was concluded that each species of pollen possesses a predominant antigen and one or more subordinate antigens. E. WALZER.

Dermatology

Evaluation of Intramuscular Injections of Specific Extracts in the Treatment of Acute Poison Ivy Dermatitis. Howell, J. B.: Ann. Allergy **5**: 219, 1947.

Twenty-three patients with acute poison ivy dermatitis were given four intramuscular injections of poison ivy extract during the course of their eruption. Seventeen others received from one to four injections of a placebo which consisted of crude liver, strontium bromide, or proteolac. Similar local therapy was administered to both groups. There was no significant difference in symptomatology or in the rate of healing in the two groups. The average time required for recovery in each case was approximately thirteen days in both series. Only three of eight brands of ivy extract yielded positive patch tests in patients highly sensitive to ivy. Other ivy-sensitive patients patch tested with these preparations showed only feeble reactions. The administra-

tion of poison ivy extract is contraindicated for treatment of acute Rhus dermatitis. Commercial poison ivy preparations vary widely in their ability to produce skin reactions. E. WALZER.

Cutaneous Reaction Units. Wodehouse, R. P.: Ann. Allergy **5**: 203, 1947.

A simple numerical system of recording reaction intensities in direct skin testing and in passive transfer experiments is suggested. Considering the unit of cutaneous reaction as a wheal 1 mm. in diameter surrounded by the erythema with a diameter of the same in excess, cutaneous reactions may be expressed by multiplying the wheal diameter by the excess of the erythema diameter over that of the wheal diameter in millimeters. Hence, in the formula $(e - w)\ w = n$, e equals the over-all diameter of the erythema, w the diameter of the wheal, and n represents the number of cutaneous reaction units. E. WALZER.

Allergic Eczematous Contact Type Dermatitis Caused by DDT. Leider, M. J.: J. Invest. Dermat. **8**: 125, 1947.

The patient had developed a rash one week after spraying his garden with a commercial preparation containing DDT. When seen by this observer nine months later, he was covered with a generalized eczematous eruption. Patch tests with 5 per cent DDT in acetone and with the commercial preparation were positive. Control patch tests with irritating substances were negative. When fifty unselected cases were patch tested with 5 per cent DDT in acetone, they failed to respond. Positive reactions to 5 per cent DDT in acetone are regarded as specific. E. WALZER.

Antihistaminic Substances and Experimental Sensitizations. Mayer, R. L.: Ann. Allergy **5**: 113, 1947.

Pyribenzamine in doses of 0.1 mg. per kg. protected more than 50 per cent of actively sensitized guinea pigs aaginst fatal anaphylaxis. Guinea pigs sensitized by subcutaneous injections with hog serum developed strong inflammatory processes at the sites of subsequent intracutaneous injections of the antigen, generalized dermatitis medicamentosa, and redness and edema of the ears, eyes, nose, and extremities. The subcutaneous administration of pyribenzamine in doses of 10 to 25 mg. per kg. produced a temporary remission of these symptoms within thirty-five minutes, and the effect lasted up to five hours. Contact dermatitis in animals made hypersensitive to p-phenylenediamine was diminished in 20 to 50 per cent by the subcutaneous injection of 20 mg. per kg. pyribenzamine begun fifteen minutes after retreatment with the antigen, and continued three times a day for two days. Pyribenzamine afforded greater protection when applied locally as a 5 per cent base in sesame oil than when administered subcutaneously. Similarly, the contact dermatitis of guinea pigs sensitized to 2,4-dinitrochlorobenzene, according to the method of Landsteiner and Chase, was found to be less severe when pyribenzamine was administered subcutaneously in doses of 10 mg. per kg. body weight fifteen minutes before injection of the antigen, and again five times in the subsequent forty-eight hours. Pyribenzamine appears to be a valuable adjunct in the detection of histamine or histaminelike substances in various allergic mechanisms. It is suggested that histamine or histaminelike substances are not only a factor in anaphylaxis and closely related manifestations, but also play a role in experimental contact dermatitis. E. WALZER.

Otorhinology and Ophthalmology

Excessive Self-Medication With Naphazoline Hydrochloride ("Privine Hydrochloride"). Mertins, Paul: J. A. M. A. **134**: 1175, 1947.

Three cases of continued rhinitis and nervousness attributable to the use of privine hydrochloride are recorded. In two of the patients withdrawal of the medication was followed by a return of the nasal mucosa to the normal state. The third patient went into collapse three days after withdrawal of the drug. The blood pressure fell to 85/50 and, at the patient's insistence, the privine hydrochloride was resumed. Gradual withdrawal of the drug is now being attempted. Sedatives, steam inhalations, and mild protein silver packs are helpful in easing the patient's discomfort for the first few days after the withdrawal of the privine. Other types of nose drops, the antihistaminics and sulfonamides, are of no value at this time. Ephedrine by mouth often increased the patient's nervousness. F.

Changes in the Nasal Function Associated With Variations in Emotional State and Life Situation. Holmes, T. H., Goodell, H., Wolf, S., and Wolff, H. G.: Trans. Am. Acad. of Ophth. & Otol. Page 449, May-June, 1947.

Experiments are presented demonstrating that nasal disturbances may be related to stressful situations in life. During the course of nasal examinations, the experimental subjects were exposed to a series of environmental threats. Their nasal reactions in terms of nasal obstruction, secretion, swelling and redness of mucous membrane (Tallqvist scale) were noted and recorded. Noxious stimulation of the nose with fumes of ammonium carbamate resulted in hyperemia, swelling of the nasal structures with hypersecretion and obstruction. This was considered to be a reaction of defense, an effort at shutting out, washing away and ejection of the offending substance. A similar reaction was obtained in a susceptible subject during an attack of hay fever.

A more specific threat, not directed at the respiratory passages, in the form of an intense headache induced by constricting the head in a tight-fitting steel crown, resulted in a similar reaction. Such reactions could also be produced by means of situational threats which did not involve the application of physical trauma. Under narcosynthesis, it was possible, in some patients, to induce nasal symptoms at will by discussing sensitive topics unsympathetically. Thus, in response to situational threats, changes may occur in nasal function similar to those taking place in response to locally applied noxious stimuli. C.

Ragweed Reagins in Nasal Secretions. Samter, M., and Becker, E. L.: Proc. Soc. Exper. Biol. & Med. **65**: 140, 1947.

The nasal secretions of four normal subjects and of ten ragweed-sensitive patients with marked skin reactivity and demonstrable circulating reagins were obtained by inserting cotton plugs saturated with 10 per cent sodium chloride solution into the nostrils. Passive transfer sites were prepared with 0.1 ml. of Seitz-filtered secretions and tested twenty-four hours later. The nasal secretions of seven of ten ragweed patients contained ragweed reagins. E. WALZER.

Allergic Deafness. Fuchs, A. M., and Almour, R.: New York State J. Med. **47**: 1397, 1947.

Recurrent attacks of deafness in an adult allergic male were traced specifically to the ingestion of fish, tomato, and ketchup, or exposure to tobacco smoke and face powder. On three occasions when complete deafness followed

exposure to one of these allergens, return of normal hearing followed the subcutaneous injection of epinephrine. The findings were confirmed by audiometric readings. It is believed that the allergic factors in this case produced a repeated and successive hydrops of the perilymphatic space which temporarily exerted pressure upon Corti's organ through the endolymph causing impairment of auditory function. C.

Miscellaneous Allergies

Allergy to Virus and Rickettsial Vaccines. I. Allergy to Influenza A. and B. Vaccines in Children. Ratner, B., and Untracht, S.: J. A. M. A. **132**: 899, 1946.

A group of 108 allergic children up to eighteen years of age with diagnoses of asthma, eczema, urticaria or hay fever were tested with influenza vaccine (Type A. and B.). About 0.02 ml. of undiluted vaccine was introduced intracutaneously, and the reactions were read immediately and at intervals up to one hour. A positive reaction consisted of a wheal at least 1 cm. in diameter with an erythema of at least 3 cm. Control tests were performed with formaldehyde 1:2,000 and merthiolate 1:40,000. Eleven children showed strong positive reactions. One developed an attack of asthma two hours after the test, and another experienced a constitutional reaction when 0.5 ml. of influenza vaccine was administered subcutaneously. All of the positive reactors to vaccine showed strong reactions to egg white. Doubtful reactions to the vaccine consisting of an erythema 2 cm. in diameter but no whealing occurred in thirty-nine children. Of these, ten showed suspicious reactions to tests with ovomucoid, egg yolk, or egg white, but were not clinically egg sensitive. Three of the doubtful group gave a history of intolerance to egg, but were negative by skin test. The remaining twenty-six doubtful reactors were negative clinically and by skin test. Among the fifty-nine negative reactors to vaccine, five responded with suggestive reactions to egg proteins, but these reactions were not considered significant. Among a control series of twenty-eight normal children, eight showed suggestive reactions to the vaccine which were attributed to nonspecific irritants or to sensitivity to formaldehyde. Hence, although 10.2 per cent of the series were sensitive to egg white, in only 4.6 per cent of the cases could the administration of influenza vaccine be regarded as potentially hazardous. Preliminary intracutaneous testing with undiluted influenza vaccine is recommended before the administration of a prophylactic dose. In the presence of a moderate or marked reaction, the vaccine should be cautiously administered. A systemic response to a skin test with influenza vaccine is a contraindication for further use. E. WALZER.

Allergy in Brucellosis. Leon, A. P., and Sosa, J.: Am. J. Public Health **37**: 1033, 1947.

Brucella infected guinea pigs and rabbits were tested with saline suspensions of Brucella abortus and melitenses. The guinea pigs began to show positive reactions beginning one month after infection, and the rabbits at two months. In the guinea pigs, the reactions with homologous and heterologous antigens were of equal intensity, whereas the rabbits showed more intense reactions to the homologous antigen. Dale studies on the uteri of sensitized rabbits were positive with both types of the Brucella suspensions. In supposedly normal persons skin tested with the bacterial suspensions, 6.4 per cent gave positive reactions to the weakest test dose, and 26.1 to the strongest. Proved

cases of Brucellosis showed positive reactions to the weakest dose in 41.1 per cent. One hundred per cent of the cases gave reactions to the strongest dose. Homologous antigens elicited stronger skin reactions in the majority of cases. In cases of Brucellosis, positive skin reactions appeared one month after the onset of the disease, and steadily increased in intensity for five or more years. The intensity of the skin reaction diminished after a series of sixteen to nineteen intracutaneous injections of the Brucella suspension, when this desensitization was begun six or more months after the onset of the disease. Clinical evaluation without controls suggested that patients with Brucellosis recovered in from two to five months when intracutaneous desensitization wase carried out.

Lung Calcifications and Histoplasmin-Tuberculin Skin Sensitivity. Sontag, L. W., and Allen, J. E.: J. Pediatrics **30**: 657, 1947.

Among young people living in the Mississippi River area, 27 to 83 per cent have demonstrable pulmonary calcification which previously was regarded as indicative of healed primary tuberculosis. Less than 50 per cent have positive tuberculin tests. In the present study, 170 normal Ohio subjects 1 to 19 years of age had serial chest x-rays and were tested intracutaneously with tuberculin and histoplasmin. Of these, 60.6 per cent had demonstrable pulmonary calcification, 44.7 per cent were histoplasmin positive, and 15.3 per cent were tuberculin positive. Thirty-three children with pulmonary calcification showed negative reactions to tuberculin and to histoplasmin; one had a positive skin test to blastomycin, and one was positive to both blastomycin and haplosporangin. These results confirm the findings of previous investigators that the incidence of histoplasmin sensitivity among young people with pulmonary calcification is greater than the incidence of tuberculin sensitivity. A study of siblings revealed a familial tendency toward pulmonary calcification, but not toward histoplasmin sensitivity. J. SHERMAN.

Sensitivity to Penicillin Resulting in Abscess Formation. Call, R. A., and Gilbert, R. A.: J. A. M. A. **134**: 1475, 1947.

A 38-year-old soldier had received repeated series of intramuscular penicillin injections. Each of these series was followed in from one week to two months by the appearance of abscesses at the injection sites. While under hospital observation, an abscess occurred following the injection of sterile aqueous solution of penicillin, whereas sterile water injected into the opposite hip failed to cause a similar reaction. Penicillin from the same test vial was injected into another individual without ill effect. F.

Allergic Peritonitis. Sison, A. B. M., Dionisio, S. A., and Chavez, P. C.: J. A. M. A. **134**: 1007, 1947.

A 31-year-old Filipino female was admitted to the hospital complaining of epigastric fullness and severe paroxysmal abdominal pain accompanied by nausea, vomiting, and some respiratory distress. The patient had had four similar episodes during the preceding four years. Each attack was accompanied by ascites, leucocytosis, and peripheral blood and ascitic fluid eosinophilia as high as 57 per cent. The syndrome had always occurred in association with pregnancy or the puerperium. The symptoms simulated those of an acute appendicitis, and an appendectomy had been performed at the time of the first attack. Portal cirrhosis, chronic nephritis, tuberculous peritonitis, para-

sitism, trichinosis, and periarteritis nodosa were considered and ruled out in the differential diagnosis. There was a strong familial and personal history of allergy. Because of the apparent relationship between the attacks and the pregnancies, the estrin-progestin mechanism was suspected as a possible cause of the trouble. Injection of estrone was followed in twenty-two hours by an attack of abdominal pain which was relieved by epinephrine. Progesterone was subsequently given without recurrence of the pain. The authors do not attempt to draw any conclusions as to the exact relationship of the estrin-progesterin mechanism and the attacks. Because of the strong familial and personal history for allergy, coupled with the eosinophilia and the relief observed after epinephrine, the syndrome was believed to be a peritonitis of allergic etiology. F.

Intradermal and Complement Fixation Reactions Elicited by Various Antigens in Persons Infected With Onchocerca Volvulus. Bozicevich, J. Donovan, A., Mazzotti, L., Diaz, F. A., and Padilla, E.: Am. J. Tropic. Med. **27**: 51, 1947.

A single skin biopsy showed microfilariae in 40 per cent of a group of eighty-one persons diagnosed clinically as having Onchocercas volvulus nodules. An immediate whealing response to an intracutaneous injection of Onchocerca volvulus antigen was obtained in 96 per cent of the patients having nodules. Antigens from three other filariids produced whealing reactions in from 57 to 83 per cent of these patients. Up to 33 per cent of persons harboring other helminths showed positive reactions on testing with the four filariid antigens although many of these subjects had never been exposed to filariids. K.

Toxic, Allergic, and "Myxedematoid" Symptoms in the Treatment of Thyro-Toxicosis With Antithyroid Substances (Thiourea, Thiouracil, Methyl-thiouracil). Lundback, K.: Acta Med. Scandinav. **124**: 266, 1946.

Agranulocytosis, when it is total and sudden in onset following long-continued treatment with a drug, may sometimes be regarded as an allergic manifestation. Such cases are often fatal and differ from toxic agranulocytosis occurring at the onset of treatment. The author reports a fatality following treatment with methylthiouracil. Other allergic manifestations observed among his patients treated with antithyroid substances included: drug fever, which could be reproduced by provocative doses of the drug; skin eruptions (urticaria, morbilliform and maculopapular eruptions); and conjunctivitis H.

Sympathectomy as an Antiallergic Measure. Coca, A. F.: Ann. Allergy **5**: 95, 1947.

Selective abolishment of familial nonreaginic food sensitivities resulted following sympathectomy in two patients. Major and minor allergen sensitivities were abolished by this procedure, whereas desensitization with histamine had produced a loss of only minor allergen sensitivity. Limited sympathectomy and abstinence from pulse-accelerating foods cured a third patient, a 10-year-old child, of stammering, tic, and irritability. In a fourth patient, the probably antiallergic effect of sympathectomy was forecast by ganglion block with procaine on one occasion, and procaine and alcohol on another. It is suggested that the procaine block test be utilized in the selection of cases for sympathectomy in patients showing sensitivities to only a few foods.

E. WALZER.

B. C. G. Vaccination in Scandinavia. Twenty Years of Uninterrupted Vaccination Against Tuberculosis. Birkhaug, G. K.: Am. Rev. Tuberc. **55**: 234, 1947.

Intracutaneous or transcutaneous B.C.G. vaccination of nonreactors to tuberculin has been a public health measure in Norway, Sweden, and Denmark since 1926. Nonreactors have been proved to be more susceptible to tuberculous disease than positive reactors. Ninety-five per cent of tuberculin-negative persons showed a positive response to a Mantoux test six to eight weeks after B.C.G. vaccination. The average duration of tuberculin sensitivity following vaccination was four years, but sensitivity may disappear after one year. Since 1940, over 550,000 Scandinavians have been vaccinated. "The incidence of destructive tuberculous disease is one-tenth, nondestructive tuberculosis less than one-fourth, and deaths from tuberculosis 1:5.6 among the vaccinated group as compared to the nonvaccinated general population in Oslo." Results have been similar elsewhere in Norway, in Sweden, and in Denmark. With the multiple puncture technique, about 5 per cent of vaccinated persons develop local abscesses. The common experience has been that the vaccine is harmless and highly effective. K.

Intradermal Test for Sensitivity to Iodopyracet Injection, or "Diodrast." Alyea, E. P., and Haines, C. E.: J. A. M. A. **135**: 25, 1947.

Among 1,675 patients who received intradermal skin tests with iodopyracet, 86 per cent showed negative reactions. Of the 239 with positive skin reactions, thirty-four (16 per cent) experienced generalized reactions, while only 4 per cent of the negative group had such reactions. There were 105 patients in the entire group with positive personal histories for allergy. Twelve of these showed positive skin reactions and of these, 70 per cent experienced generalized reactions following the intravenous administration of the drug. In patients with negative personal histories and positive skin reactions, only 13.6 per cent experienced generalized reactions. In patients with negative personal histories and negative skin reactions, 3.5 per cent developed constitutional reactions. These findings indicate that patients with positive personal histories of allergy and positive skin reactions to "diodrast" are most likely to have generalized reactions to the drug. "Diodrast" should therefore not be administered to patients in this group. However, systemic reactions may occur in cases with negative skin and ophthalmic reactions and precautions must be taken whenever the drug is given. F.

Anaphylaxis

Production of Acute Rheumaticlike Heart Lesions in Mice. Moore, F. J., Ridge, G. K., Huntington, R. W., Hall, E. M., Griffith, G. C., and Knowles, R. G.: Proc. Soc. Exper. Biol. & Med. **65**: 102, 1947.

One group of mice was given three intraperitoneal injections of egg white at two-day intervals, and a fourth injection four to twenty-one days later. Survivors were sacrificed one week after the last injection. A second group of animals received one intraperitoneal dose and three intravenous injections at weekly intervals. In a third group, the first three injections at weekly intervals were intraperitoneal, and the fourth was intravenous. All mice in the latter two groups were sacrificed within one hour of the final injection. Lesions resembling those described by Rich in rabbits and similar to acute rheumatic carditis in man were observed. There were focal areas of acute vascular and perivascular degeneration of reticular and collagenous connective tissue with complete fibrinoid degeneration of arteriolar walls, hydropic degeneration, and

disruption of myocardial fibrils, perivascular cellular infiltration, cellular infiltrations at the base of the papillary muscle, verrucous lesions of mitral leaflets, and pathologic fusion of aortic cusps. However, untreated control animals revealed some "rheumatic stigmata," though to a slight degree. Most of the tissue changes were ascribed to the second and third doses of egg white. No relationship was found between the intensity of clinical anaphylaxis and the severity of pathologic lesions. E. WALZER.

The Reticulo-Endothelial Origin of the Bone Marrow Plasma Cells in Hypersensitive States. Kolouch, F., Good, R. A., and Campbell, B.: J. Lab. & Clin. Med. **32**: 746, 1947.

Six rabbits were given injections of varying doses of *Streptococcus viridans* over a period of several months. Another group received a single subcutaneous injection of 10 c.c. of broth culture of the same organism suspended in agar. The animals in the second group were shocked with a broth culture of *Streptococcus viridans,* and serial rib biopsies were made. Examination of the bone marrow of the first group of animals showed a marked increase in the bone marrow plasma cells, as well as an increase in the reticular plasma cells in some animals. Study of the bone marrow of the second series revealed that sensitization had produced an increase in the number of reticular plasma cells. Within two hours after the animals were shocked nuclear contraction and cytoplasmic condensation occurred in the reticular plasma cells. Continuation of these changes resulted in the production of small plasma cells of the Marchalko type which were abundant four days after shocking. Animals sensitized to egg white and subsequently shocked showed bone marrow changes identical with those of the bacterial sensitive rabbits. Similar, reticular cells and plasma cells in various stages of development were noted in the peripheral blood of a patient with serum sickness. "It is suggested that this morphological cycle is associated intimately with the production of antibodies." E. WALZER.

The Bronchodilator Action of Compounds Structurally Related to Epinephrine. Siegmund, O. H., Granger, H. R., and Lands, A. M.: J. Pharmacol. & Exper. Therap. **90**: 254, 1947.

By means of histamine atomization and lung perfusion tests, the relative efficacy of various sympathomimetic amines in antagonizing histamine was studied in guinea pigs. The drugs tested were nor-epinephrine, epinephrine, and the N-isopropyl (Isuprel), N-sec. butyl, and isopropyl homologues of 1(3′,4′-dihydroxyphenyl)-2-aminoethane. Isuprel and the sec. butyl derivative were more effective than epinephrine in counteracting histamine spasm. Analysis of the results suggested that the alcoholic hydroxyl on the beta carbon of the side chain and an alkyl group on the nitrogen determined the bronchodilator activity of these compounds. Acute toxicity studies in mice indicated that branching of the N-alkyl group markedly reduced toxicity.

Use of Crotalin in the Prevention of Anaphylactic Shock in Guinea Pigs. Frank, D. E.: Ann. Allergy **5**: 156, 1947.

For fourteen days prior to and after sensitization with horse serum, crotalin (rattlesnake venom) was administered daily in increasing doses intra-abdominally to twenty-three guinea pigs. When shocking doses of horse serum were administered intravenously to these animals, fifteen survived. In a series of five animals sensitized with horse serum and subsequently treated with crotalin, four were protected against anaphylactic shock. Fifty per cent of the animals

that received a single large dose of crotalin the day after sensitization survived when tested two weeks later. The administration of a single large dose of crotalin one day prior to testing failed to protect any of ten animals. It is suggested that crotalin liberates histamine, and its administration in small increasing doses or in a single large dose subsequent to sensitization produces an increased tolerance for histamine. E. WALZER.

Miscellaneous

Disseminated Lupus Erythematosus and Diffuse Scleroderma. Baehr, G., and Pollack, A. D.: J. A. M. A. **134**: 1169, 1947.

Although fibrinoid degeneration of collagen is a common finding in disseminated lupus erythematosus, scleroderma, rheumatic fever, rheumatoid arthritis, serum sickness, periarteritis nodosa, thromboangitis obliterans, and other conditions, these diseases should not be considered to have a common etiologic factor such as allergy. There are definite differences between lupus erythematosus and periarteritis nodosa. In the latter, the degeneration of collagen is limited to the vessel walls and is always accompanied in the acute stage by a definite cellular inflammatory reaction in the adventitia and media. Eosinophiles are prominent in these reactions. In lupus erythematosus, however, the vascular involvement is only one phase of the general connective tissue degeneration. The fact that 95 per cent of lupus erythematosus cases occur in females aids in differentiating it from periarteritis nodosa. In rheumatic fever, the collagen degeneration may be similar to that seen in lupus erythematosus, but it is less extensive and less frequently involves the arterial walls. A typical finding in rheumatic fever is the cellular response which produces Aschoff bodies. Leucopenia, evidence of renal damage, and a high preponderance of female involvement aid in differentiating lupus erythematosus from rheumatic fever. The rash of lupus erythematosus may not become evident early in the disease; in fact, it may never become manifest. F.

Studies on Filariasis. V. Serological Relationships Between Antigenic Extracts of Four Nematodes. Warren, V. G.: Am. J. Hygiene **45**: 299, 1947.

Hyperimmune rabbit sera were prepared against the adult worms of the filariids *Wuchereria bancrofti, Dirofilaria immitis,* and the larvae of the nematode *Trichinella spiralis.* Complement-fixation tests were carried out with these sera and antigens and also with an extract of *Litomosoides carinii,* the filarial worm of the cotton rat. The antigens tested were found to react not only with the homologous antisera, but also with the heterologous sera. Unlike the other two sera, the immune serum for *Dirofilaria immitis* reacted at dilutions almost as high with the heterologous antigens as with its own antigen. *Trichinella spiralis* antigen reacted as strongly with *Dirofilaria immitis* antiserum as with its homologous serum, despite the fact that Trichinella is not a filariid. These results are consistent with previous reports of the occurrence of a common antigen in nematodes. K.

Anesthetic Action of the Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in the Skin of Human Beings. Leavitt, M. D., and Code, C. F.: Proc. Soc. Exper. Biol. & Med. **65**: 33, 1947.

The anesthetic action of benadryl was studied in the skin of ten normal subjects and compared with that of procaine hydrochloride. Benadryl in dilutions of 1:500 to 1:20,000 in physiologic saline was injected intracutaneously on the

forearms and wheals from 1.5 to 2.0 cm. in diameter were raised. Pain thresholds of injected sites were measured by an algesimeter. Sensation in intact skin was repeatedly compared with that in injected skin. Intracutaneous saline did not appreciably alter the pain threshold in control sites. Benadryl in dilutions up to 1:5,000 consistently produced complete anaesthesia lasting at least three minutes. Similar anesthetic effects were produced by benadryl 1:500 and procaine 1:200; benadryl 1:5,000 and procaine 1:800; and benadryl 1:20,000 and procaine 1:3,200. Six of ten persons injected with benadryl 1:100 experienced an immediate burning sensation at the site, and four of these exhibited a delayed reaction consisting of sloughing and ulceration. In dilutions of 1:500, benadryl administered to two subjects caused transient burning, pain, redness, and slight edema which disappeared within six hours. No attempt to correlate the anaesthetic and antihistaminic properties of benadryl was made.

E. WALZER.

Effects of Pyribenzamine and Benadryl on Chick Embryo and on Vascular Phenomena Induced by Normal Serum. Netter, E.: Proc. Soc. Exper. Biol. & Med. **65**: 90, 1947.

When pyribenzamine and benadryl in amounts of 2.5 mg. in 1.0 ml. buffered solution were dropped slowly on three-day chick embryos, almost complete immediate bradycardia resulted. Within two minutes, there was complete cardiac stoppage and death of the embryo. Hemorrhages in the embryo or in the vascular network were observed in some instances. In amounts of 0.5 to 1.0 mg., these drugs caused bradycardia and rarely transitory cardiac stoppage, whereas in doses smaller than 0.1 mg. no visible changes occurred. Nontoxic doses of pyribenzamine or benadryl when administered prior to or concomittant with Forssman antibodies (normal rabbit serum) failed to prevent the vascular phenomena described by Wetebsky and his associates. It is suggested that the chick embryo may be used to advantage in the study of the relative toxicity of antihistaminic compounds.

E. WALZER.

Reagins: Preliminary Report on Experimental Evidence in Support of a New Theory of Their Nature. Immunochemical Studies of Reagin I. Miller, H., and Campbell, D. H.: Ann. Allergy **5**: 236, 1947.

The quantitative effect of the reagins of egg-sensitive patients on the precipitative reaction between ovalbumin and rabbit antiovalbumin serum was studied. Reaginic sera of egg-sensitive patients were added to crystalline ovalbumin in varying dilutions and incubated at room temperature for two hours. Rabbit antiovalbumin serum was then added and the mixture incubated at room temperature for two hours and at 4° C. for forty hours. The precipitate obtained was analyzed for protein by the Folin-Ciocalteu method. It was found that the reaginic sera increased the amount of precipitate. Reaginic serum from pollen sensitive individuals employed as a control failed to produce an increase in the amount of protein precipitated. It is concluded that the reagins in egg-sensitive serum are in some way incorporated in the ovalbumin-rabbit antiovalbumin precipitation.

B. SIEGEL.